TRENDS, CORRELATES, AND PATTERNS OF CONCURRENT SUBSTANCE USE OF PRESCRIPTION STIMULANTS IN THE UNITED STATES

by

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ABSTRACT

Objective: The purpose of this study is to fill the knowledge gap regarding nonmedical prescription stimulant use. The study has three aims: 1) to explore the temporal trends of prescriptions, nonmedical use, and Emergency Department (ED) visits for specific prescription stimulants; 2) to investigate the source of the misused stimulants and whether different sources correspond to different risk profiles; and 3) to identify subgroups among nonmedical prescription stimulant users by their concurrent problematic substance use in different age groups.

Method: National surveys across 2006 to 2011 were used in all three aims. Aim 1 used National Disease and Therapeutic Index (NDTI), National Survey on Drug Use and Health (NSDUH), and Drug Abuse Warning Network (DAWN) and ordinary linear square regression to assess the temporal trends in frequency of prescription, nonmedical use and ED visits involving Adderall and methylphenidate. Aim 2 used logistic regression models to compare the socio-demographic, mental health and behavioral problems and stimulant use-related problems according to source of nonmedically used stimulants using the NSDUH data. Aim 3 used latent class analysis to examine patterns of past-year problematic substance use in participants reporting past-year nonmedical prescription stimulant use in adult and adolescent participants in the NSDUH.

Results: Analyses for Aim 1 revealed that temporal trends in treatment visits involving stimulants do not correspond to trends in nonmedical use and ED visits. Prescription visits for Adderall did not change over time, while nonmedical use and ED visits grew dramatically among adults. The major source of misused stimulants

was a physician for both Adderall and methylphenidates. Aim 2 showed that sources of misused stimulants were associated with onset, recency and severity of stimulant use, with illegal and physician sources both associated with earlier onset, greater odds of recent use and meeting the diagnostic criteria for stimulant use disorder. Aim 3 identified a four-class model in both adults and adolescents including a *Low substance* class, a *Prescription drug* class, an *Alcohol/Marijuana* class, and a *Multiple substance* class. Individuals in the three classes other than the *Low substance* class were more likely to report psychological and social outcomes. **Conclusions:** The findings highlight the need to target drug diversion as a preventive strategy and a more nuanced preventive and treatment program that takes into account differences in risk profiles and needs of subgroups of nonmedical users of stimulants.

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Chapter 1: Introduction

1.1. Problem statement

Nonmedical use of prescription drugs ranks as the second most common class of illicit drug use in the United States, with an annual average of 15.7 million people aged 12 or older having used prescription drugs nonmedically between 2005 and 2011 (SAMHSA, 2012). Nonmedical use can be defined as use without a doctor's prescription, use in greater amount or for a longer period than prescribed, or use for reasons other than the doctor's recommendation (Blanco et al., 2007). Among the prescription drugs, prescription stimulants have been commonly used nonmedically especially among young adults and adolescents (NIDA, 2009).

Prescription stimulants mainly refer to stimulants prescribed for treatment of a variety of medical conditions, including narcolepsy, obesity, and mainly attention-deficit/hyperactivity disorder (ADHD) (Greenhill et al., 2002). Methylphenidate (Ritalin), dextroamphetamine (Dexedrine) and mixed-salts amphetamine (Adderall), considered as first-line pharmacotherapy for the treatment of ADHD, are sold in different brand names. There is increasing public concern and research interest regarding the growing nonmedical use of these ADHD stimulants in the past decades (Arria et al., 2008; McCabe et al., 2007a; McCabe et al., 2005; Teter et al., 2005; Teter et al., 2006). In 2011, 1.1 million Americans aged 12 or older used prescription stimulants nonmedically in the past year (SAMHSA, 2012).

There are several adverse physical, psychological and social consequences related to nonmedical use of prescription stimulants. First, the abuse potential of these stimulants has long been recognized, resulting in their classification as schedule

II substances in the Controlled Substances Act (CSA) (Drug Enforcement Administration, 2003). Both Adderall and methylphenidate work on dopamine system, which is involved with the addiction reward pathway (Pliszka et al., 1996). Second, there are reports regarding the increased cardiovascular risks associated with the use of these stimulants (Gould et al., 2009; Sichilima and Rieder, 2009; Westover and Halm, 2012), leading the US Food and Drug Administration (FDA) to put a black box warning on Adderall (FDA, 2006). Third, the use of these ADHD stimulants may increase risks of psychosis or mood disorder (Chakraborty and Grover, 2011a; Mosholder et al., 2009). The health and social burden of the increased nonmedical use of stimulants is reflected in the increase in Emergency Department (ED) visits involving ADHD stimulants between 2005 and 2010 (SAMHSA, 2013a).

1.1.1. Trends of prescription of prescription stimulants

The legal production of methylphenidate (Ritalin) and amphetamine (Adderall, Dexedrine) in the U.S. has grown remarkably since 1990 (Safer et al., 1996; White et al., 2006). The rate of their distribution is carefully monitored by the Drug Enforcement Administration (DEA), which establishes quotas for schedule II controlled substances by analyzing past sales, inventory, anticipated need, and market trend data. The growing demand for prescription stimulants in the U.S. is evidenced by the fact that the methylphenidate quota increased from 1,768 kilograms in 1990 to 96,750 kilograms in 2013, and the amphetamine quota increased from 417 to 49,000 (Drug Enforcement Administration, 2013). The rise in prescription and consumption of these medicines could be attributed to several factors, including an increased diagnosis of ADHD (Olfson et al., 2003; Safer, 2000; Safer et al., 1996;

Zito et al., 2003) and increased duration of treatments (Safer, 2000), and possibly increased misuse rates of these medications.

The increased availability of ADHD stimulants have long been suspected to be associated with increased nonmedical use of these drugs (Cohen et al., 2006; McCabe and Boyd, 2005), evidenced by numerous college based and national studies showing remarkable increase of nonmedical use (Arria et al., 2008; McCabe et al., 2005; SAMHSA, 2009a; Teter et al., 2006). However, there is so far no study examining the relationship of temporal trends in prescriptions and nonmedical use of ADHD stimulants.

1.1.2. Trends in nonmedical use of prescription stimulants

Abundant evidence has shown that nonmedical use of prescription stimulants mainly affect young individuals (Johnston, 2003a-b; McCabe et al., 2004; SAMSHA, 2008b), especially college students (McCabe et al., 2005; SAMHSA, 2009a; White et al., 2006). In college-based studies the lifetime prevalence of prescription stimulant misuse and abuse has ranged from 3% to 16% (Babcock and Byrne, 2000; Hall et al., 2005; Teter et al., 2003). The misuse of these medications is not limited to college age youth. Between 3.3% to 4.5% of middle school and high school youth also report nonmedical use of prescription stimulants (McCabe and Teter, 2007; McCabe et al., 2004).

Limited data exist regarding the trends in nonmedical use of specific stimulants. Past research mainly combined all prescription stimulants together (McCabe et al., 2005; SAMHSA, 2009a; White et al., 2006) or focused on one specific prescription stimulant, most often methylphenidates (Babcock and Byrne,

2000; Safer et al., 1996; Teter et al., 2003). To the best of our knowledge, only one study has examined the trend of nonmedical use of different prescription stimulants, in which nonmedical use of Adderall proved to be more prevalent than nonmedical use of methylphenidates among college students (Teter et al., 2006). Thus, there is a need for more information on trends in nonmedical use of specific stimulants, and the association of such use with the trend of prescription or adverse consequences of these drugs.

1.1.3. Sources of prescription stimulants

A large number of studies have examined the characteristics and correlates of nonmedical prescription stimulant use; however, few studies have examined the sources of misused stimulants. Most of these studies identified a friend or relative as the major source for misused prescription stimulants (DeSantis and Hane, 2010; Garnier-Dykstra et al., 2012; McCabe et al., 2006b; White et al., 2006). A recent study revealed that 89% of college students reported obtaining the misused stimulants from a friend or significant other (DeSantis and Hane, 2010). In addition, the high availability of stimulants over the Internet has been documented by a previous study and has been suspected to be an increasing source of prescription drugs (Schepis et al., 2008) However, overall, Internet remains a minor source of nonmedically used stimulants (Inciardi et al., 2010). Examining how sources vary across the socio-demographic spectrum would provide useful information for design of preventive interventions and even individual treatment planning. For example, knowing whether use of a specific source might signal a greater likelihood of other

substances use, persistence of stimulant use problem may be a useful guide for treatment planning.

1.1.4. Profiles of nonmedical prescription stimulants users

As discussed above, nonmedical use of prescription stimulants mainly affects young adults and adolescents (Arria et al., 2008; Kroutil et al., 2006; McCabe et al., 2007a; McCabe et al., 2005; McCabe and Teter, 2007; SAMHSA, 2009a; Teter et al., 2005; Teter et al., 2006). In national surveys such as Monitoring the Future (MTF) and the National Survey on Drug Use and Health (NSDUH), college students were found to be twice as likely to report nonmedical use of prescription stimulants than their counterparts not attending college (Johnston, 2003; SAMHSA, 2009a). College students who reported nonmedical prescription stimulant use were also more likely to be male, white, members of fraternities and sororities, and to have earned lower grade point averages (Arria et al., 2008; McCabe et al., 2005; Teter et al., 2005; Teter et al., 2006). However, no sex difference was found in adolescent users (Herman-Stahl et al., 2007; McCabe et al., 2004). Regardless of age, nonmedical users of prescription stimulants were more likely to report use of alcohol, cigarettes, marijuana, ecstasy, cocaine and deviant behaviors (Arria, 2008; Herman-Stahl et al., 2006, 2007; McCabe et al., 2006a; McCabe et al., 2004, 2006b; SAMHSA, 2009a; Teter et al., 2005; Teter et al., 2006). The reasons for using stimulants nonmedically included improving attention, partying, reducing hyperactivity, and improving grades (Garnier-Dykstra et al., 2012; McCabe et al., 2004; Teter et al., 2005; Teter et al., 2006; White et al., 2006).

The variations in the social and health consequences of stimulant misuse, concomitant use of other substances and the different motives reported by youth who use these drugs nonmedically suggests that these users are not a homogenous group. However, little is known about possible subgroups among these youth as most past research has compared nonmedical prescription stimulant users to non-users regarding their other substance use and risky behaviors (McCabe et al., 2007a; McCabe et al., 2005; McCabe and Teter, 2007; SAMHSA, 2009a; Teter et al., 2005; Teter et al., 2006; White et al., 2006). A better understanding of this heterogeneity may enhance understanding of the epidemiology of nonmedical use of stimulants and contribute to prevention and treatment efforts. It is conceivable that some youth misuse stimulants as study aids or to self-medicate their attention problems; whereas, others may be using these drugs recreationally along with alcohol or other illegal drugs. These groups would be expected to have different substance use profiles as well as different health, social and academic outcomes.

1.2. Study aims

Previous studies have shown an increasing trend in stimulant prescriptions and in nonmedical use of these prescription stimulants; however, the role of prescription (i.e. availability of these drugs) in nonmedical use is rarely examined. The 2006 FDA black box warning on Adderall makes examination of these trends especially timely. To address this question, the first aim of this project was to examine the recent trends in prescription and nonmedical use of two commonly prescribed and misused stimulants: methylphenidate and Adderrall. More specifically

we examined quarterly trends in prescriptions, nonmedical use, and ED visits associated with these drugs in adults and adolescents.

Second, we capitalized on the wide variations of sources of stimulants to better characterize the profiles of nonmedical prescription stimulant users. In addition, we further examined the relationship between the sources of these stimulants and the onset, recency, and severity of stimulant use problems. This analysis sheds light on the role of source as an indicator of seriousness and persistence of stimulant misuse and varied treatment needs of individual stimulant users based on their source of stimulants.

Lastly, whether there exist heterogeneous subgroups among stimulant users with regard to their concurrent substance use patterns is examined as the third aim of this study. We will further examine the socio-demographic characteristics, mental health and behavioral of subgroups of participants thus identified.

The study has the following specific aims and hypotheses:

Aim 1: To assess the association between three national trends from 2006-2011: treatment visits involving stimulants using the National Disease and Therapeutic Index (NDTI) data, nonmedical use based on the National Survey on Drug Use and Health (NSDUH) data, and emergency department (ED) visits using Drug Abuse Warning Network (DAWN) data. Analyses will be conducted separately for methylphenidate and Adderall and for adults and adolescents.

Hypothesis 1: The increasing trends in the prescription of specific stimulants will be associated with the increased nonmedical use of the same prescription stimulants, which will be associated with increased ED visits.

***Aim 2*:** To investigate whether different sources of misused stimulants are associated with different socio-demographic, psychological and behavioral profiles and stimulant use problems using 2006-2011 NSDUH data.

Hypothesis 2: Individuals who report obtaining their stimulants from illegal sources will have distinct socio-demographic, psychological and behavioral profiles and are more likely in engage in other illegal behavior compared to other sources.

Aim 3*:* To explore subgroups of individuals who use prescription stimulants nonmedically according to concurrent drug use profiles using latent class analysis and to identify socio-demographic, mental health and behavior correlates of these subgroups using the NSDUH data.

Hypothesis 3: Nonmedical stimulant users are comprised of at least two classes of participants: one class with a greater prevalence of concurrent problematic substance use and maladaptive behaviors, and another with lower prevalence of concurrent substance use and associated problems.

1.3.Overview of chapters

1.3.1. Chapter 2

Chapter 2 aims to investigate recent temporal trends in prescriptions, nonmedical use, and Emergency Department (ED) visits of two most commonly prescribed stimulant medications (Adderall and methylphenidate) using three representative national surveys conducted between 2006-2011: National Disease and Therapeutic Index (NDTI), a survey of office-based practices, National Survey on Drug Use and Health (NSDUH), a population survey of substance use, and Drug

Abuse Warning Network (DAWN), a survey of ED visits. The associations of the three trends among adults and adolescents are examined using Ordinary linear square (OLS) regression.

1.3.2. Chapter 3

Chapter 3 aims to investigate the relationship between sources of misused stimulants and socio-demographic, psychological and behavioral profiles of nonmedical prescription stimulant users, and onset, recency and severity of stimulant use problems using the 2006-2011 NSDUH data. Multinomial logistic regression was used to examine these associations using both unadjusted and adjusted regression models.

1.3.3. Chapter 4

Chapter 4 addresses Aim 3 using data on NSDUH adult and adolescent participants who reported past-year nonmedical use of ADHD stimulants. We used latent class analysis (LCA) to examine patterns of past-year problematic substance use (met any criteria for abuse or dependence). Multivariate latent regression was used to assess the association of socio-demographic, mental health and deviant behavior characteristics with the latent classes.

1.3.4. Chapter 5

Chapter 5 summarizes the main findings from each study aim (i.e., Chapters 2-4), describes study limitations and strengths, and discusses the public health implications of the current study.

Chapter 2: Prescriptions, Nonmedical Use, and Emergency Department Visits Involving ADHD Stimulants

Abstract

Importance: There are growing concerns about the nonmedical use of stimulants medications. However, little is known regarding the temporal trends in prescription, nonmedical use and emergency department (ED) visits involving these medications in the United States.

Objectives: To investigate recent trends in prescriptions, nonmedical use of, and ED visits for Adderall (dextroamphetamine-amphetamine) and methylphenidate, two commonly prescribed stimulant medications, in adults and adolescents.

Design, Setting, and Participants: We used data from three representative national surveys conducted between 2006-2011: National Disease and Therapeutic Index (NDTI), a survey of office-based practices, National Survey on Drug Use and Health (NSDUH), a population survey of substance use, and Drug Abuse Warning Network (DAWN), a survey of ED visits.

Main Outcomes and Measures: Quarterly treatment visits (NDTI), nonmedical use (NSDUH), and ED visits (DAWN); source of misused stimulants (NSDUH), and reasons for ED visits (DAWN).

Results: In adolescents, prescriptions of Adderall and methylphenidate decreased over time; nonmedical use of Adderall remained stable and nonmedical use of methylphenidate declined for 54.4% in 6 years. ED visits involving either medication remained stable among adolescents. In adults, prescription visits for Adderall did not change over time, while nonmedical use went up by 67% and ED visits went up by

156% and were strongly associated. Prescriptions, nonmedical use, and ED visits involving methylphenidate did not change in adults. For both drugs, the major source across age groups was a friend or relative. In two-thirds of the cases, the friend or relative had obtained the medication through prescriptions from a physician.

Conclusions: Trends over time in the number of prescriptions for stimulants do not correspond to trends in reports of nonmedical use and ED visits. Increases in problems related to stimulant misuse may not relate simply to temporal prescribing trends. Physician prescriptions were the major source of nonmedical stimulant drug use, suggesting that prevention strategies should target drug diversion routes as well as education on the adverse consequences of stimulants.

1. Introduction

The abuse potential of prescription stimulants, commonly used for treatment of attention deficit/hyperactivity disorder (ADHD), has long been recognized, resulting in classification of these drugs as schedule II substances in the Controlled Substances Act (CSA) (Drug Enforcement Administration, 2003). Nonmedical use of these medications has increased in recent years (Arria et al., 2008; McCabe et al., 2007a; McCabe et al., 2005; Teter et al., 2005; Teter et al., 2006) and student population is especially vulnerable to the problem. In national surveys such as Monitoring the Future (MTF) and the National Survey on Drug Use and Health (NSDUH), college students were twice more likely to report nonmedical use of prescription stimulants than their counterparts not attending college (Johnston, 2003a-a; SAMHSA, 2009a). In another study among middle and high school students, 4.5% reported nonmedical stimulant use, of whom, 23.3% reported being approached to sell, give, or trade these drugs (McCabe et al., 2004). The potential consequences of nonmedical use included other substance use, psychiatric comorbidities, criminal involvement, cardiovascular conditions and other adverse health outcomes among individuals using stimulants (Arria et al., 2008; Gould et al., 2009; Higashi et al., 2011; McCabe et al., 2005; NIDA, 2009b; Sichilima and Rieder, 2009).

The US Food and Drug Administration (FDA) put a black box warning on Adderall in 2006 due to its associated cardiovascular risks (Food and Drug Administration, 2006). There is some evidence that Adderall prescriptions declined after the FDA warning. In one study, treatment visits for Adderall declined from 36%

in 2004 to 24% in 2008 (Kornfield et al., 2013). Nevertheless, Emergency Department (ED) visits involving ADHD medications tripled from 2005 to 2010 (SAMHSA, 2013a). Similarly, in another study based on the Poison Control Center's National Poison Data System, calls related to ADHD medication misuse in teenagers rose by 76%, much faster than calls for other substances abused by adolescents (Setlik et al., 2009).

Furthermore, prescription trends and trends in nonmedical use may reflect different population groups. Although the majority of ADHD medications are prescribed for children and adolescents, most of the nonmedical ADHD stimulant users are young adults (Arria et al., 2008; McCabe et al., 2005; McCabe et al., 2007c; Teter et al., 2005; Teter et al., 2006; White et al., 2006). Also, ED visits for nonmedical use of ADHD stimulants have showed distinct patterns for adolescents and adults (SAMHSA, 2013a). Trends in prescription, nonmedical use, and ED visits for specific ADHD stimulants have rarely been examined separately for adults and adolescents. An improved understanding of nonmedical use of ADHD stimulants in these two populations would be a valuable step in the development of effective prevention and treatment interventions.

This study aimed to elucidate these trends and their relationships by examining temporal trends in prescriptions, nonmedical use, and ED visits involving Adderall and methylphenidate among adults and adolescents between 2006 and 2011. We assessed the associations of these trends using three nationally representative datasets: National Disease and Therapeutic Index (NDTI), a survey of office-based practices, National Survey on Drug Use and Health (NSDUH), a population survey

of substance use, and Drug Abuse Warning Network (DAWN), a survey of emergency department (ED) visits. Additionally, we examined the reported sources of nonmedically used Adderall and methylphenidates, and the reasons for ED visits involving these medications.

2. Method

2.1. Samples

Data on prescription frequency were obtained from NDTI, a nationally representative audit of office-based physicians conducted by IMS Health. The NDTI uses a two-stage sampling procedure and collects data on patient contacts from approximately 4,300 physicians randomly selected within strata defined by specialty and geographic area, generating approximately 350,000 annual contact records. We limited our analyses to the approximately 85% of contacts generated through office visits. Our primary unit of analysis was a visit during which Adderall or methylphenidate was prescribed or continued—referenced to below as a treatment visit. There were 26,469 contacts involving ADHD medications for patients aged 12 years and older, including 18,143 for Adderall and 8,654 for methylphenidate.

Data on nonmedical use of medications was obtained from NSDUH public use data for 2006 to 2011 (N=338,495). The NSDUH is an annual cross-sectional survey sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA) and is designed to provide estimates of the prevalence of alcohol and drug use in the household population of the United States, 12 years of age and older. The survey employs an independent multistage area probability

sample for each of the 50 states and the District of Columbia. The response rate for household screening ranged from 87% to 91% and for completed participant interviews from 74% to 76% across the 6 years. Detailed information about the sampling and survey methodology of NSDUH are found elsewhere (SAMHSA, 2007, 2008, 2009, 2010, 2011, 2012). Among the NSDUH 2006–2011 participants, there were 7,151 nonmedical Adderall users and 3,197 nonmedical methylphenidate users.

Data on ED visits involving Adderall and methylphenidate were obtained from DAWN for 2006 to 2011 (N= 1,648,992). DAWN is sponsored by the SAMHSA, and consists of a network of over 250 hospitals that monitors drug-related visits to hospital EDs. The DAWN data are collected directly from the medical records of patients treated in the EDs and the reports are submitted electronically using the Electronic Hospital Emergency Reporting System (eHERS), a customized system developed specifically for DAWN. Detailed information about the sampling and survey methodology of DAWN can be found elsewhere (SAMHSA, 2011). Between 2006 and 2011, a total of 9,181 visits involved Adderall and 2,483 involved methylphenidate.

2.2. Assessments

Prescription frequency in NDTI was assessed by a physician visit during which ADHD stimulants were prescribed or continued. We focused on two groups of medications: Adderall (including Adderall and Adderall XR) and methylphenidates (including Ritalin, Ritalin SR, Ritalin LA, Concerta, Methylin, Methylin ER, Metadate). NDTI links each drug therapy to a specific six-digit taxonomic code

capturing diagnostic information similar to the International Classification of Diseases 9th Revision (ICD-9).

Nonmedical use of methylphenidate in NSDUH was assessed using the following question: "Have you ever, even once, used Ritalin or Methylphenidate that was not prescribed for you or that you took only for the experience or feeling it caused?" A similar question was asked regarding the nonmedical use of Adderall. Each question was followed by a question about the time of the most recent use. We defined past-year nonmedical ADHD stimulant use by a positive response to the questions and further indicated that the last use was within 12 months.

NSDUH participants who reported using ADHD stimulants nonmedically in the past 30 days were asked a series of questions on how they had obtained these drugs. The sources ascertained included friends/relatives (got for free, bought from them or took without asking), direct physician source (got from one doctor or doctor shopping), illegal source (buying from a drug dealer or via internet), other source (fake prescriptions or some other way), and multiple sources (have more than two of the above-mentioned sources). We combined the source variables into five larger categories as some of the specific sources were endorsed by very few participants. Participants who reported obtaining the stimulant from a friend or relative for free were asked how that friend or relative had obtained the drug (secondary source). Those who reported either primarily or secondarily from a physician were recorded as having obtained the drug from a physician source.

Information on ED visits in DAWN included medication or substances of abuse that might contribute to the visit based on the medical record. We focused on

ED visits involving methylphenidate or Adderall. DAWN also assessed the reasons for the ED visits. We categorized the reasons for ED visits into three categories based on a previous study (Olfson et al., 2003): nonmedical use (including suicide attempt, overmedication, accidental ingestion and malicious poisoning), adverse reaction, and others.

2.3. Statistical analyses

We restricted the samples from all three datasets to participants aged 12 years and older in order to have consistent age ranges for the three data sources. Physician visits, nonmedical use and ED visits involving methylphenidate and Adderall were examined quarterly from 2006 to 2011 separately for adults (aged 18 or above) and teenagers (aged 12-17). Ordinary linear square (OLS) regression was used to assess the temporal trend in frequency of prescription, nonmedical use and ED visits across quarters. Time was the independent variable of interest in these models. The associations between prescription frequency and nonmedical use and between nonmedical use and ED visits were also examined using OLS regression. We tested OLS models for autocorrelation across time using Durbin-Watson tests (Durbin and Watson, 1950) and we further reported results adjusting for autocorrelations using Newey-West standard errors if the Durbin-Watson test for autocorrelation produced inconclusive results.

Next, we examined the distribution in sources of methylphenidate and Adderall used in the past 30 days including primary and secondary sources across different age. In order to examine whether time modifies the relationship between nonmedical ADHD stimulant use and source of the misused drug, we divided these

users into three mutually exclusive groups: 1) nonmedical Adderall users only, 2) nonmedical methylphenidate users only and 3) nonmedical Adderall and methylphenidate users (as a large proportion of participants reported using both drugs). Reasons for ER visits were analyzed separately for Adderall and methylphenidate among adolescents (age 12-17) and adults (aged 18 and above).

To obtain nationally representative quarterly frequency estimates, data were weighted to reflect the complex design of the NSDUH and DAWN samples and were analyzed by Stata 13.0 software (StataCorp, 2013). We used Taylor series estimation methods as implemented in STATA svy commands to obtain proper standard error estimates for the cross-tabulations and logistic regressions.

3. Results

3.1. Demographics characteristics

The demographic characteristics of individuals included in the three samples are presented in Table 1. Based on the NDTI data, individuals who were prescribed ADHD stimulants were more likely to be male than female (Adderall: 58.5%, methylphenidate: 53.7%), non-Hispanic whites (Adderall: 85.4%, methylphenidate: 87.0%), and most commonly in the 12-17 years age range (Adderall: 43.0%, methylphenidate: 30.9%). Notably, while 26% of methylphenidate visits included adults age 50 years and older, only 8.1% of Adderall visits fell in this age range.

Based upon the NSDUH data, past-year nonmedical users of both Adderall and methylphenidate were more likely to be male (Adderall: 55.6%, methylphenidate: 53.7%), aged 18-25 years (Adderall: 59.7%, methylphenidate:

50.8%), and white (Adderall: 86.4%, methylphenidate: 86.8%; Table 1). The proportion of nonmedical Adderall users of all users increased from 13.3% in 2006 to 20.2% in 2011, while the proportion of nonmedical methylphenidate users in each year remained relatively stable.

ED visits resulting from Adderall use, as reported in DAWN (Table 1) were more frequent among females (54.9%), those aged 35-54 years (26.4%), and whites (86.8%). ED visits involving methylphenidate use were equally common in both sexes (50.0%), more frequent in those aged 12-17 years (26.8%), and in whites (91.1%). There was an increasing trend over 6 years for ED visits involving Adderall and methylphenidate use.

3.2. Temporal trends among adolescents

Adderall treatment visits among adolescents decreased from 479,000 in the first quarter of 2006 to 223,000 visits in the last quarter of 2011. Since Adderall visits in adolescents showed inconclusive results, we adjusted this model for autoregression (regression coefficient [B]= -9.24, standard error [SE]=1.57, $p<0.001$) (Figure 1A). Nonmedical Adderall use and ED visits, however, did not change appreciably during this period. Methylphenidate treatment visits in adolescents also decreased from 191,000 in the first quarter of 2006 to 113,000 visits in the last quarter of 2011 (B=-3.47, SE=0.68, $p<0.001$). Nonmedical use of methylphenidate decreased significantly in this period from 2.06% in the first quarter of 2006 to 0.94% in the last quarter of 2011 (B=-0.04, SE=0.01, $p<0.001$). The prevalence of ED visits involving methylphenidate for adolescents did not show a significant change over time (Figure 1A). There was a statistically significant association between methylphenidate visits

and nonmedical use of methylphenidate (B=0.01, SE=0.002, p=0.001), other associations between the temporal trends were all non-significant (Appendix Table 1).

3.3. Temporal trends among adults

Adderall treatment visits among adults changed little in the study period, from 379,000 in the first quarter of 2006 to 364,000 visits in the last quarter of 2011 (Figure 1B). However, the prevalence of past-year nonmedical use of Adderall in adults increased over the study period, from 0.73% in the first quarter of 2006 to 1.22% in the last quarter of 2011 (B=0.10, SE=0.01, p<0.001). ED visits involving Adderall in adults similarly increased from 0.34% in the first quarter of 2006 to 0.87% in the last quarter of 2011 (B=0.02, SE=0.003, p<0.001) (Figure 1B). Furthermore, there was a statistically significant association between nonmedical Adderall use and ED visits involving Adderall in this age group over the study period (B=0.68, SE=0.13, p <0.001). Physician visits, nonmedical use and ED visits involving methylphenidate did not change appreciably during the study period (Appendix Table 1).

3.4. Sources of nonmedically used stimulants

Friends or relatives were the major primary source of nonmedically used stimulants, regardless of age groups and medication type, contributing 59.9% to 68.5% of all sources of nonmedically used stimulants (Table 2). In addition, we found a physician's prescription comprised almost two-thirds of secondary drug source for both drugs across age groups, ranging from 59.3% to 75.4%. We then created three mutually exclusive groups of nonmedical ADHD stimulant users in

order to examine the effect modification of time. The analyses showed that participants who used both Adderall and methylphenidate nonmedically were more likely to obtain the drug from physician sources, regardless of whether this was the primary or secondary source (OR=1.57, 95% CI=1.11, 2.21, P=0.009), compared to those only using Adderall alone. There was no evidence of an effect modification over the study period (P=0.087), indicating that the sources of misused drugs did not change appreciably across time.

3.5. Reasons for ED visits

ED visits due to nonmedical use of Adderall or methylphenidate among adults constituted more than one-third of all drug-related ED visits (Adderall: 30.3%, methylphenidate: 35.9%) (Table 3). In addition, for adolescents, 46.2% of ED visits involved nonmedical use of Adderall, and 37.3% involved methylphenidate. It is noteworthy that adverse reactions due to medical use of methylphenidate constituted about half of the ED visits among adolescents.

4. Discussion

This study had three principal findings. First, prescription visits did not necessarily show coincident changes with prevalence of nonmedical use. For instance, the prevalence of nonmedical use of Adderall in adults increased remarkably while prescription trends of this drug remained stable. Second, nonmedical use of Adderall increased by 67% and associated ED visits went up remarkably by 156% in adults while both trends remained unchanged in adolescents, suggesting different trends in different age groups. Third, physician was the major

source for the misused stimulants regardless of types of stimulants or age group. Also, those who used both Adderall and methylphenidate nonmedically were more likely to obtain the drugs from physician sources compared to those who used Adderall only.

There was a sharp increase in ADHD treatment rate in the U.S. in the late 1990s (Olfson et al., 2003) and this increase continued until recent years (Visser et al., 2014; Zuvekas and Vitiello, 2012). Yet, our study showed that physician visits for Adderall and methylphenidates among adolescents aged 12-17 declined from 2006 to 2011. One explanation for these discrepant findings is that the role of psychostimulants in treatment of ADHD has changed in recent years. Stimulants were used in 96% of visits in 2000, but only 87% of visits in 2010 (Garfield et al., 2012). Another explanation is the introduction of new stimulants such as Vyvanse which has cut into the market for Adderall and methylphenidates.

Our study further showed that the reduction in methylphenidate prescription visits for adolescents was associated with decreased nonmedical use (although a causal association cannot be inferred). In contrast, nonmedical use of Adderall in adults increased, while prescription visits did not grow. The former finding is consistent with the theory that decreased availability of these medications through physician prescriptions may reduce nonmedical use of the drug (Komro and Toomey, 2002). This conclusion, however, is not supported by the contrasting trends in Adderall prescriptions and nonmedical use in adults.

The differences in the temporal trends in nonmedical use of Adderall and methylphenidate open to a number of potential explanations, including differences in

pharmacological properties and in social factors. The extended-release formulation of Adderall has a longer duration of action than methylphenidate, producing a more steady effect (Markowitz et al., 2003). Furthermore, although both Adderall and methylphenidate increase CNS dopamine by blocking the dopamine transporter, Adderall additionally increases noreponephrine, which is associated with improved cognitive function (Pliszka et al., 1996). Since cognitive enhancement is the most commonly reported reason for nonmedical use of prescription stimulants (DeSantis and Hane, 2010; Teter et al., 2006; White et al., 2006), differences between Adderall and methylphenidate with regard to cognitive enhancement properties could partially explain Adderall's increased popularity, especially among college students (Teter et al., 2006).

Social context in which the stimulant is used may also provide an explanation for nonmedical use trends. A 2010 multi-approach study of college students who reported nonmedical use of stimulants found that these students had limited knowledge of the physical or psychological effects of the drugs (DeSantis and Hane, 2010). Also, about 36% of the stimulant users believed using Adderall could help them to be "smarter" and 89% of them got the drug from their friends. The reputation of Adderall on college campuses as "not harmful" and as means of "getting smart" may contribute to the increased rate of nonmedical use among adults.

Our study also found that adult ED visits involving Adderall showed a strong correlation with increased nonmedical use in adults. This finding is consistent with a previous DAWN report that found marked increase in ED visits involving ADHD

medications in adults, but not adolescents (SAMHSA, 2013a). Our study further revealed that this trend is limited to Adderall use among adult population.

Consistent with past research, our study found that a friend or relative was the major source for the nonmedically used ADHD stimulants (DeSantis and Hane, 2010; Garnier-Dykstra et al., 2012; McCabe et al., 2006b; Teter et al., 2006; White et al., 2006). Our study further found that among those who obtained the drug from a friend or relative, more than 70% of them obtained their drug legitimately through a doctor's prescription. This finding suggests that drug diversion plays a crucial role in nonmedical ADHD stimulant use. A study found that 61.7% of college students diagnosed with ADHD reported diverting their prescription stimulants (Garnier et al., 2010). Additionally, those who used both Adderall and methylphenidate nonmedically were more likely than those with nonmedical Adderall use only to report obtaining the drug from physician sources, implying a heavier role of doctor shopping among these population.

The limitations of this study should be considered in interpreting the results. A major limitation was that the three datasets (NDTI, NSDUH, and DAWN) were not linked, which limited our capability to make further conclusion about the associations. For instance, we were not able to assess whether nonmedical use and ED visits happened among the same individuals who were prescribed these medications. Thus, causal inference from these data may be subject to "ecological fallacy". Second, physician visits for methylphenidate and Adderall cannot directly represent the availability of these medications. Different dosages of medications may have been filled in each visit. Third, NSDUH used responses regarding the source of

nonmedically used stimulants in general to ascertain the source in those who reported using specific stimulants. Beginning in 2006, NSDUH asked specific question about nonmedically used Adderall; whereas, before 2006, nonmedically used Adderall was specified by participants' report. Thus, the source question was asked among all nonmedical prescription stimulant users except for Adderall users. To assess the impact of this decision, we repeated the analyses limiting the data to year 2006 and after. The results were similar to the main analysis (data not shown), suggesting that changes in the ascertainment method did not influence the findings of the study. Fourth, the NSDUH relies on self-reports, whereas NDTI and DAWN rely on physicians' reports, which may be vulnerable to recall bias. Finally, effects of the shifts in medical care policy or in drug market share may not be fully captured by these data.

5. Conclusion

In the context of these limitations, the findings highlight the urgent need for public health campaigns to target drug diversion from legitimately prescribed users as physician prescriptions constitute the main source of nonmedically used ADHD stimulants. Clinicians should discuss the proper dispensation of the medications with their patients and educate them about their responsibilities regarding drug diversion.

Table 1. Characteristics of participants in samples examining trends in prescriptions, non-medical use and emergency department visits involving Adderall and methylphenidate using data from 2006-2011.

	Prescriptions in treatment visits[b] (National Disease and Therapeutic Index)				**Nonmedical use (National Survey on Drug Use and Health)**				**Emergency department visits (Drug Abuse Warning Network)**			
	Adderall (n=15,125)		Methylphenidate (n=8,654)		Adderall (n=7,151)		Methylphenidate (n=3,197)		Adderall (n=9,181)		Methylphenidate (n=2,483)	
Characteristics	N	Wgt% (95%CI)	N	Wgt% (95%CI)	N	Wgt% (95%CI)	N	Wgt% (95%CI)	N	Wgt% (95%CI)	N	Wgt% (95%CI)
Gender												
Male	8846	58.5(57.7,59.3)	4649	53.7(52.7,54.8)	3855	55.6(53.9,57.3)	1654	53.7(50.8,56.6)	4229	45.1(41.6,48.2)	1246	50.0(43.5,56.6)
Female	6102	40.3(39.6,41.1)	3889	44.9(43.9,46.0)	3296	44.4(42.7,46.1)	1543	46.3(43.4,49.2)	4948	54.9(51.4,58.4)	1237	50.0(43.4,56.6)
Age[a]												
12-17	6511	43.0(42.3,43.8)	2672	30.9(29.9,31.9)	1836	16.3(15.3,17.4)	795	14.1(12.7,15.7)	1084	10.9(8.6,13.8)	725	26.8(22.1,31.1)
18-25	3319	21.9(21.3,22.6)	1113	12.9(12.2,13.6)	4771	59.7(57.6,61.6)	2030	50.8(47.9,53.7)	1881	19.4(16.8,22.3)	497	19.7(16.5,23.4)
26-34	1727	11.4(10.9,11.9)	955	11.0(10.4,11.7)	368	14.9(13.1,16.8)	239	19.7(16.5,23.3)	1762	18.7(16.1,21.6)	448	21.8(10.1,17.0)
35-49	2340	15.5(14.9,16.1)	1661	19.2(18.4,20.0)	154	7.2(6.0,8.7)	114	10.4(8.6,12.4)	2598	26.4(23.7,28.9)	626	26.5(11.5,21.9)
≥50	1227	8.1(7.7,8.6)	2253	26.0(25.1,27.0)	22	1.9(1.1,3.4)	19	5.0(2.7,9.0)	1856	24.9(21.0,29.2)	187	7.0(16.0,23.6)
Race												
White	12912	85.4(84.8,85.9)	7533	87.0(86.3,87.7)	5974	86.4(84.8,87.8)	2666	86.8(84.2,89.1)	6266	86.8(82.7,89.9)	1672	91.1(86.9,94.1)
Black	1190	7.9(7.4,8.3)	512	5.9(5.4,6.4)	189	2.3(1.9,2.8)	68	2.6(1.5,4.3)	666	7.7(5.4,10.9)	167	3.2(2.0,5.0)
Hispanic	584	3.9(3.6,4.2)	271	3.1(2.8,3.5)	502	6.8(5.9,7.3)	226	6.6(5.1,8.3)	473	4.7(29,7.6)	146	4.8(2.7,8.4)
Others	439	2.9(2.6,3.2)	337	3.9(3.5,4.3)	486	4.6(3.8,5.4)	237	4.1(3.0,5.4)	125	0.8(0.5,1.4)	40	0.9(0.4,2.4)
Year												
2006	3018	20.0(19.3,20.6)	1737	20.1(19.2,20.9)	962	13.3(12.1,14.5)	520	16.2(14.4,18.3)	862	8.9(5.8,13.5)	293	8.3(4.8,13.9)
2007	2900	19.2(18.5,19.8)	1477	17.1(16.3,17.9)	1048	13.8(12.6,15.1)	487	14.8(12.7,17.3)	1275	12.1(7.3,19.2)	400	19.1(12.0,29.1)

2008	2237	14.8(14.3,15.4)	1309	15.1(14.4,15.9)	1025	14.4(13.2,15.7)	509	17.2(15.0,19.6)	1625	14.4(9.4,21.6)	491	16.8(10.3,26.3)
2009	2522	16.7(16.1,17.3)	1423	16.4(15.7,17.2)	1257	18.7(17.2,20.3)	553	18.6(16.3,21.1)	2047	18.2(12.0,26.8)	549	18.0(12.1,26.0)
2010	2240	14.8(14.2,15.4)	1455	16.8(16.0,17.6)	1385	19.6(18.3,21.1)	581	18.2(16.0,20.7)	1883	19.5(13.0,28.1)	440	16.2(10.1,25.0)
2011	2208	14.6(14.0,15.2)	1283	14.8(14.1,15.6)	1474	20.2(18.5,21.9)	547	15.0(13.2,16.9)	1489	26.9(16.5,40.8)	310	21.6(12.6,34.3)

a. The age ranges for the public-access DAWN data are slightly different that those in other datasets. Participant ages in DAWN were categorized into ages 18-24, 25-34, 35-54, and ≥55 years.

Table 2. Reasons for past-year emergency department visits involving Adderall or methylphenidate using the Drug Abuse Warning Network, 2006–2011.

Characteristics	Adolescents				Adults			
	Adderall		Methylphenidate		Adderall		Methylphenidate	
	N	Wgt%(95%CI)	N	Wgt%(95%CI)	N	Wgt%(95%CI)	N	Wgt%(95%CI)
Nonmedical use	621	46.2(36.5,56.1)	539	37.3(30.1,45.1)	2521	30.3(26.9,33.9)	610	35.9(29.7,42.6)
Adverse reaction	450	30.4(23.3,38.6)	651	51.1(44.0,58.2)	2817	38.5(34.2,42.9)	486	25.5(19.2,33.0)
Others	517	23.4(18.0,29.9)	173	11.6(8.2,16.0)	2328	31.3(27.9,34.8)	558	38.7(31.5,46.4)

Table 3. Sources of stimulants for past-month nonmedical use of Adderall and methylphenidate using the National Survey on Drug Use and Health, 2006-2011.

Sources	Adderall		Methylphenidate	
	N	Wgt%(95%CI)	N	Wgt%(95%CI)
Adolescent (Primary source)				
Friend or relative	166	62.5(54.1,70.2)	144	59.9(51.2,68.0)
Physicians	32	12.1(8.0,17.9)	36	14.7(10.3,20.7)
Illegal	23	9.6(6.1,14.9)	21	9.1(6.4,12.8)
Others	13	6.1(3.2,11.2)	13	5.4(2.5,11.3)
Multisources	31	9.7(6.0,15.5)	31	10.9(6.9,16.8)
Adolescent (Secondary source)	24	16.3(10.4,24.6)	23	28.8(20.6,38.7)
Friend or relative	68	66.6(55.5,76.5)	55	59.3(48.2,69.6)
Physicians	7	4.0(1.5,10.4)	6	9.9(4.4,20.6)
Illegal	19	13.1(6.5,24.5)	20	4.8(1.7,13.0)
Others				
Adult (Primary source)				
Friend or relative	681	68.5(64.1,72.5)	540	66.3(61.0,71.2)
Physicians	85	12.3(9.3,7.4)	92	16.7(13.0,21.2)
Illegal	80	7.4(9.7,10.1)	71	6.8(4.6,10.0)
Others	25	2.5(1.4,4.4)	20	2.2(1.1,4.3)
Multisources	82	9.4(6.8,12.8)	67	7.9(5.6,11.2)
Adult (Secondary source)				
Friend or relative	353	12.2(7.3,19.9)	56	19.9(11.9,31.5)
Physicians	51	75.4(67.9,81.6)	284	69.6(59.2,78.4)
Illegal	10	2.9(1.1,7.2)	8	2.9(1.0,7.9)
Others	49	9.5(6.3,14.1)	36	7.5(5.1,11.1)

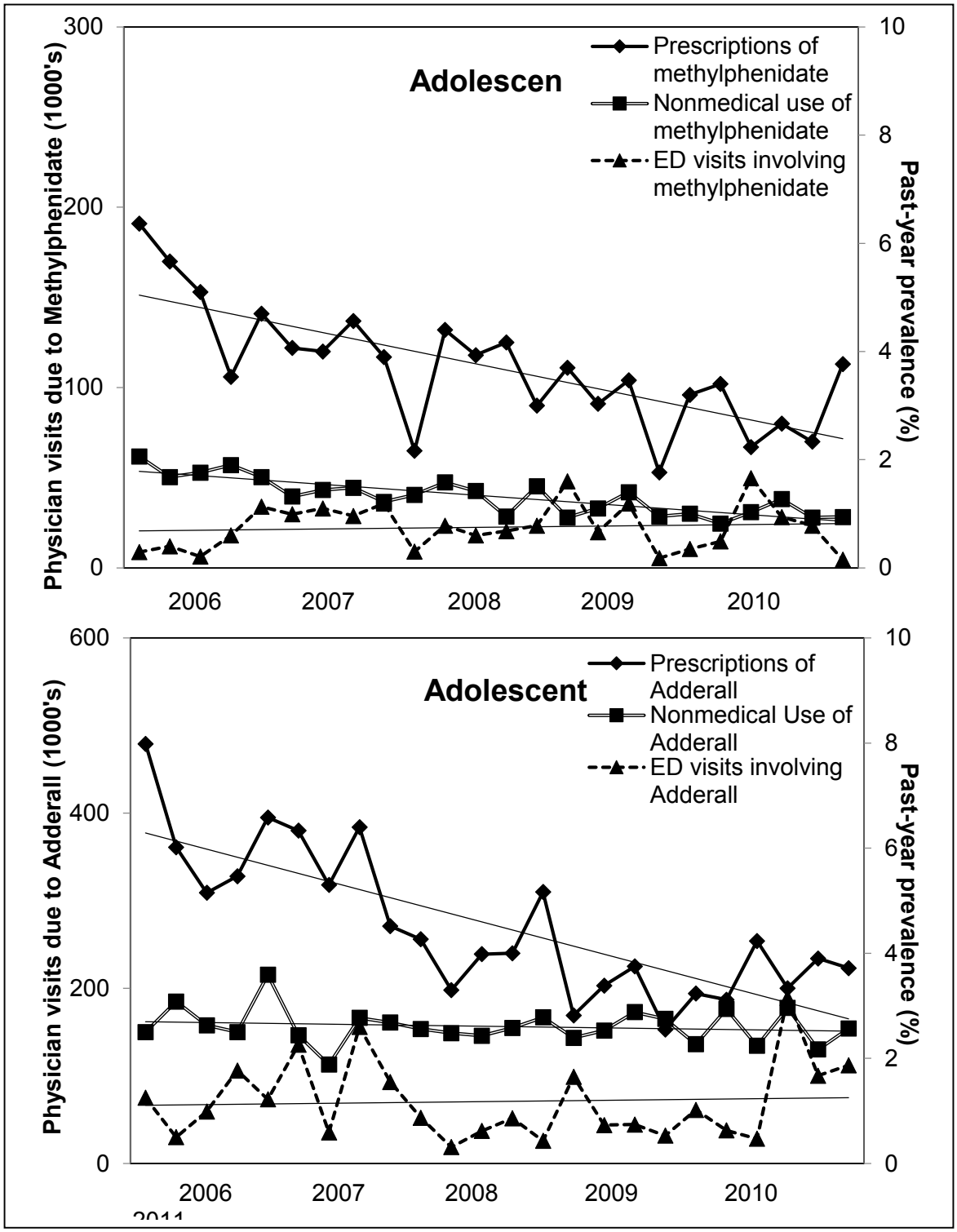

Figure 1A. Temporal trends in prescription, nonmedical use, and ED visits involving Adderall and methylphenidate among adolescents (12-17 years).
Source: IMS National Disease and Therapeutic Index®, January 2006 to December 2012, IMS Health Incorporated. All Rights Reserved.

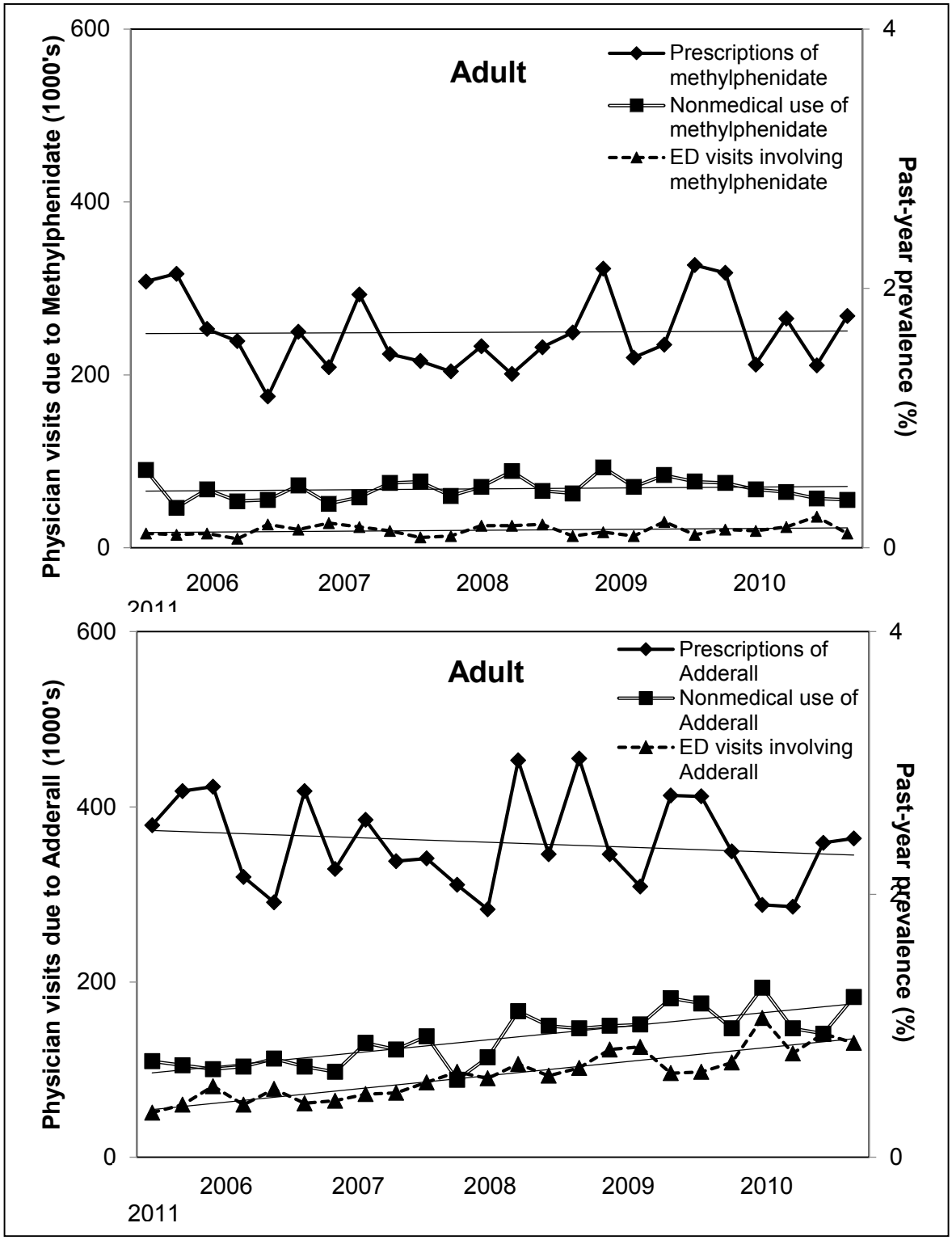

Figure 1B. Temporal trends in prescription, nonmedical use, and ED visits involving Adderall and methylphenidate among adults (18 years old or above).

Source: IMS National Disease and Therapeutic Index®, January 2006 to December 2012, IMS Health Incorporated. All Rights Reserved.

Chapter 3. Sources of Nonmedically Used Prescription Stimulants: Differences in Recency and Severity of Misuse in a Population-Based Study

Abstract

Aim: Epidemiological data indicate that nonmedical use of prescription stimulants has increased over the past decade. However, little is known regarding the source of the misused stimulants and whether different sources correspond to differences in risk profiles and associated social and health problems.

Method: Data from the 2006 to 2011 National Survey on Drug Use and Health were used. A total of 4,945 participants who used prescription stimulants nonmedically and also reported their source of misused stimulants were categorized by the source: friends/relatives source, physician source and illegal source. Logistic regression models were used to compare the socio-demographic, mental health and behavioral problems as well as stimulant use-related problems according to source of nonmedically used stimulants.

Results: The most common sources of stimulants were friends/relatives, followed by physicians and illegal sources. Compared to participants reporting friends/relatives as the source, participants reporting an illegal source were more likely to be male, unemployed, have less than a high school education, a history of criminal behavior and began using stimulants at an earlier age. Participants reporting a physician source were more likely to have mental health problems and mental health service use. Higher odds of past-month stimulant use, frequent use (≥10 days per year), drug dependence and substance service use were found in individuals reporting physician and illegal sources.

Conclusions: Identifying the source of misused stimulants can be useful in detecting distinct subgroups of nonmedical prescription stimulant users. This, in turn, may be useful in the development of tailored preventive and treatment programs, and for treatment planning for individual clients.

1. Introduction

Prescription drugs have been the second most commonly abused category of drugs behind marijuana (SAMHSA, 2012a). Prescription stimulants are a major contributor to this statistic. In 2012 about 1.2 million Americans reported using nonmedical prescription stimulants in the past year (SAMHSA, 2013a). There has been a remarkable growth in nonmedical use of these medications over the past decade particularly among young adults and adolescents (Arria and Wish, 2006; Boyd et al., 2006; McCabe et al., 2005; SAMHSA, 2009a; Teter et al., 2006).

Previous studies have made a considerable contribution to investigating the epidemiology and risk factors associated with nonmedical use of prescription stimulants. In a recent review, the prevalence of past-year nonmedical prescription stimulant use ranged from 5% to 9% in adolescents and 5% to 35% in college-age adults (Wilens et al., 2008). College population studies have shown that the nonmedical prescription stimulant users are more likely to be male, white, members of fraternities and sororities, and earning lower GPAs (McCabe et al., 2005; Teter et al., 2006). The reported motives for use in this population range from cognitive enhancement and study aid to recreational use (Teter et al., 2005; White et al., 2006). Previous studies have consistently demonstrated that nonmedical prescription stimulant users are more likely to report other substance use and involvement of risky behaviors (McCabe et al., 2007a; McCabe et al., 2005; Teter et al., 2005).

Previous studies have also revealed that a friend or relative was the major source for the nonmedically used prescription stimulants (DeSantis and Hane, 2010; Garnier-Dykstra et al., 2012; Garnier et al., 2010; McCabe et al., 2006b; White et al.,

2006). Although apparent availability of stimulants over the Internet without a prescription has been reported (Schepis et al., 2008), the Internet remains a relatively minor source for prescription drugs as a whole (Inciardi et al., 2010).

Little past research has investigated the implications of variations in specific source of nonmedically used stimulants. In particular, the implications for frequency, recency and severity of associated problems remain unexplored. This study attempted to fill the knowledge gap using data from the 2006 to 2011 National Survey on Drug Use and Health (NSDUH). More specifically, we sought to answer the following questions: 1) Do individuals reporting different sources of misused stimulants show different socio-demographic, mental health and behavioral profiles? and 2) Is the source of the nonmedically used stimulants associated with age of onset, recency and severity of nonmedical stimulant use?

2. Methods

2.1. Sample

We analyzed data from the NSDUH public use data files for 2006 to 2011 (N= 338,495). We restricted our sample to participants who reported using prescription stimulants nonmedically in the past year after excluding those who used methamphetamine only (N=4,945). We conducted the analyses combining adolescent and adult data, as our previous analyses indicated few differences in sources of nonmedically used stimulants among adolescent and adult participants of NSDUH (data not shown). The NSDUH is an annual cross-sectional survey sponsored by the Substance Abuse and Mental Health Administration (SAMHSA) and is designed to

provide estimates of the prevalence of alcohol and drug use in the household population of the United States, 12 years of age and older. The survey employs a 50-state design with an independent multistage area probability sample for each of the 50 states and the District of Columbia. African-Americans, Hispanics, and youth are over-sampled to increase the precision of estimates for these groups. The response rate for household screening ranged from 87% to 91%, and for completed interviews from 74% to 76%, across the 6 years. Survey items were administered by computer-assisted personal interviewing (CAPI) conducted by an interviewer and audio computer-assisted self-interviewing (ACASI) for sensitive questions. Use of ACASI was designed to provide respondents with highly private and confidential means of responding to questions and to increase the level of honest reporting of illegal drug use and other sensitive behaviors. Respondents were offered a $30 incentive payment for participation in the survey. Detailed information about the sampling and survey methodology of NSDUH can be found elsewhere (SAMHSA, 2007, 2008, 2009b, 2010, 2011, 2012).

2.2. Assessments

2.2.1. Nonmedical prescription stimulant use

Lifetime nonmedical prescription stimulant use was ascertained through the use of a specified list of stimulants. To aid recall, pictures of the medications were provided. The stimulants include Ritalin or methylphenidate, amphetamines, dextroamphetamine, Cylert, methamphetamine, Methedrine or Desoxyn, Dexedrine, and selected diet pills. Participants were asked: “Have you ever, even once, used [Drug name] that was not prescribed for you or that you took only for the experience

or feeling it caused?" Participants were also asked if they had used any other stimulants. We further ascertained past-year prescription stimulant use if the respondents answered positively to the above question and indicated that the time since last use was within 12 months.

2.2.2. Sources of misused stimulants

NSDUH respondents who reported using prescription stimulants nonmedically in the past 12 months were asked a series of questions on how they had obtained these drugs most recently. The 10 mutually exclusive choices were categorized into the following 3 groups: friend/relative source ("got from friend or relative for free," "bought from friend or relative" or "took friend or relative without asking"), physician source ("got from one doctor" or "got from more than one doctor"), and illegal source ("bought from drug dealer or other stranger," "bought on the internet," "wrote fake prescription," "stole from doctor's office, clinic, hospital, or pharmacy"). We excluded those who reported other source from the analyses as the source was not specified.

2.2.3. Socio-demographic characteristics

Socio-demographic variables included in the analyses were sex, age (12-17, 18-25, ≥ 26), race/ethnicity (non-Hispanic white, minorities), and annual household income (≤ $19,999, $20,000-$34,999, $ 35,000-$69,999, ≥ $70,000). For adults aged 18 and above we additionally included marital status (single, non-single), employment status (partial or full employment, unemployed, not in labor force), education (less than high school, high school, college and above).

2.2.4. Past-year criminal behaviors, mental health and substance use problems

Participants self-reported how many times they had attacked someone with the intent to seriously hurting them, how many times they had sold illegal drugs, and how many times they had stolen or tried to steal anything worth more than $50 in the past year. Consistent with past research (Martins et al., 2006; Martins et al., 2009), participants who reported any of the three behaviors were categorized as having criminal behavior (0 for none of these behaviors and 1 for engaging in these behaviors 1 time or more). Past-year arrest was created to capture involvement with the law and justice systems. Based on the number of times in the past 12 months respondents had been arrested and booked for breaking the law, without counting minor traffic violations, past year arrest was categorized as 0 for none and 1 for more than once. In a section on health care, participants were asked if in the past year they had been told by a medical doctor or health care professional that they had an anxiety disorder or depression and whether they received any mental health treatment or substance use disorder treatment in the past year. The NSDUH team created separate indicators for past-year alcohol and drug dependence based on the responses to items that assessed the Diagnostic and Statistical Manual of Mental Disorders–IV (DSM-IV) criteria for eight illicit drugs (American Psychiatric Association, 1994). A composite illegal drug dependence measure that did not include stimulants was used in this report.

2.2.5. Onset, recency and severity of nonmedical use of stimulants

Early onset of stimulant use was defined by first time of use before or at age 13, which is a similar definition as has been used in previous work (Grant and Dawson, 1998). Past-month stimulant use was ascertained by use within the past 30

days. Stimulant use disorder included both stimulant abuse and dependence, defined based on criteria specified in the DSM-IV (American Psychiatric Association, 1994). Frequency of use in the past month or year was a free response question in which participants entered the exact number of days the substance was used. We defined frequent use as using stimulant more than 10 days in the past year, consistent with past literature (Schepis and Krishnan-Sarin, 2009).

2.3. Statistical analyses

Analyses focused on exploring differences between the three past-year nonmedical prescription stimulant user groups categorized by their main source: a friends/relatives, physician, or illegal source group. The group of friends/relatives source, the largest group, was set as the reference category. We used a series of logistic regression models to compare the groups with regard to socio-demographic characteristics, mental health problems, mental health and substance disorder service use, criminal behaviors and substance dependence. Another set of models examined the onset, recency, and severity of stimulant use in each of these groups. The adjusted models were controlled for age, sex, race-ethnicity, education, marital status, employment status, household income, past-year clinician-identified depression, anxiety disorders, criminal behaviors, and arrest. Mental health and substance service use were not adjusted for due to potential collinearity with mental health variables.

All percentages reported are weighted and Taylor series linearization was used to take into account the complex survey design of NSDUH. Stata 13 was used for all analyses (StataCorp, 2013).

3. Results

3.1. Sources of nonmedically used prescription stimulants

About 7.8% (n = 24,224) of participants from NSDUH 2006-2011 reported lifetime nonmedical use of prescription stimulants, and 1.1% (n=6,384) reported use in the past year. A specific source of misused stimulants was identified by 4,945 respondents, including 3,772 adults and 1,173 adolescents. The most commonly reported specific sources were getting from a friend/relative for free (52.5%), buying from a friend/relative (17.5%), and getting from just one doctor (10.3%) (Table 1). There was a relatively small proportion of prescription stimulant users who reported getting the medication from more than one doctor (2.9%) or the internet (1.8%). When these sources were summarized into the four predefined categories, the most commonly reported sources were friends/relatives sources (75.1%), followed by physicians (11.2%), illegal sources (9.8%), and then other sources (3.9%).

3.2. Correlates of source of nonmedically used prescription stimulants

Participants reporting an illegal source were predominantly male (58.3%), while no sex difference was observed in the other two groups (Table 2). Participants reporting a physician source or illegal source were more likely to be aged 12-17 (vs aged 18-25) compared to those reporting a friends/relatives source.

Compared to the group who obtained stimulants from friends/relatives, the illegal source group was significantly less likely to be female (Odds ratio [OR] 0.48, 95% confidence interval [95% CI]: 0.32, 0.72), have college or above education (OR: 0.37, 95% CI: 0.20, 0.69) and more likely to be unemployed (OR: 2.79, 95% CI: 1.18, 6.60) The illegal source group also had higher odds of criminal behaviors (OR:

2.62, 95% CI: 1.67, 4.10), and arrest (OR: 2.27, 95% CI: 1.47, 3.49) (Table 2). The physician source group was more likely to report clinically-identified depression (OR: 1.63, 95% CI: 1.05, 2.52), an anxiety disorder (OR: 4.37, 95% CI: 2.66, 7.18) and receiving mental health treatment (OR: 2.92, 95% CI: 1.96, 4.35). Both the physician source and the illegal source groups were more likely to meet the criteria for drug dependence (physician OR: 1.73, 95% CI: 1.15, 2.61; illegal OR: 2.36, 95% CI: 1.52, 3.66) and to receive substance abuse treatment in the past year (physician OR: 2.10, 95% CI: 1.30, 3.39; illegal OR: 2.50, 95% CI: 1.49, 4.18).

3.3. Stimulant use onset, recency, and severity

In the adjusted model, the physician source group was more likely to report past-month stimulant use (aOR: 3.29, 95% CI: 2.24, 4.85), frequent use (≥10 days in the past year) (aOR: 3.07, 95% CI: 1.95, 4.82), and to meet the criteria for a stimulant use disorder (aOR: 2.75, 95% CI: 1.52, 4.97) compared to the friends/relatives source group. The illegal source group was more likely to report early onset (onset ≤ age 13) (aOR: 2.07, 95% CI: 1.02, 4.15), past-month use (aOR: 1.55, 95% CI: 1.00, 2.40), frequent use (aOR: 2.21, 95% CI: 1.45, 3.38) and to meet the stimulant use disorder criteria (aOR: 2.69, 95% CI: [1.80, 4.01) compared to the friends/relatives source group. We conducted pair-wise comparisons between the physician source and the illegal source groups. In these comparisons, the physician source group was found to be more likely to report past-month use compared to the illegal source group (P=0.002). The other comparisons were not statistically significant.

4. Discussion

To the best of our knowledge, this is the first study using nationally representative data to examine the implications of the sources of nonmedically used stimulants with regard to socio-demographic and mental health characteristics of users and also seriousness of prescription stimulant use. Consistent with past research (DeSantis and Hane, 2010; Garnier-Dykstra et al., 2012; McCabe et al., 2006; White et al., 2006), friends/relatives were the major sources of misused stimulants, constituting 78.1% of all users. In addition, the internet appeared to be a relatively minor source of prescription stimulants regardless of the fact that there is widespread prescription drug availability via websites (McCabe and Boyd, 2005; Schepis and Krishnan-Sarin, 2009). Although doctor-shopping has been recognized as a dangerous signal for prescription drug fatalities (Hall et al., 2008), only 0.7% of study population reported prescriptions from more than one doctor as the source of their nonmedically used stimulants.

Those who reported an illegal source for their stimulants were more likely than those obtaining the drug from friends/relatives to be male, unemployed, and less likely to have a higher education. They were also more than two times as likely to report criminal behaviors and an experience of being arrested. This group, however, comprised only 10.2% of all nonmedical prescription stimulant users. Consistent with this finding, other research based upon NSDUH data found that adolescents who purchased their misused prescription drugs illegally had a worse risk profile in terms of concurrent substance use and severity of prescription misuse, regardless of the classes of prescription drugs purchased (Schepis and Krishnan-Sarin, 2009).

The physician source group had markedly greater mental health burden including depression, anxiety disorder, and mental health service use compared to the friends/relatives source group. This finding could indicate the use of prescription stimulants for self-medication by some in this group. In another study, up to 50% of frequent nonmedical prescription stimulant users reported depressed mood (Teter et al., 2010). Additionally, many users self-diagnose themselves as having an attention disorder (Judson and Langdon, 2009). In a 2009 survey study, 39% of college students who misused stimulants did so with the desire to self-treat target symptom such as concentration (McCabe et al., 2009). It is also possible that the some stimulant users developed psychological problems after misusing the drugs. Many stimulants, including methylphenidates and mixed amphetamines, have been shown to increase the risk of psychosis or mania (Chakraborty and Grover, 2011; Mosholder et al., 2009). Our finding underscores the significance of screening for mental health disorders among the nonmedical prescription stimulant users, particularly among those who report obtaining these drugs from physicians.

Obtaining stimulants from physicians or via illegal methods were both strongly correlated with recent use (in the past month), frequent use (more than 10 days in the past year) as well as meeting stimulant use disorder criteria. Those obtaining these drugs via illegal methods were more likely to report an early-onset of their stimulant use. Early onset of any substance use has been found to be linked to subsequent dependence on other drugs (Anthony and Petronis, 1995); thus, it is not surprising that the illegal source group was also more likely to have other drug

dependence and substance disorder service use compared to the friends/relatives source group.

The finding that the physician source group had significantly higher odds of stimulant use problems and particularly past-month use is intriguing. It is possible that a physician is a more sustainable source of drugs, leading users who obtain their misused drug from this source to continue using, which in turn may then eventually lead to a stimulant use disorder. On the other hand, the psychological vulnerabilities of this group may contribute to the persistent use of stimulants for self-medication. The more serious and persistent nature of stimulant misuse among individuals who report obtaining their drugs from physicians points to the need for better monitoring of dispensation and use of these drugs in medical practice. In one study, almost half of physicians found it difficult to discuss the abuse potential of prescription drugs with their patients (McCabe et al., 2002). This finding suggests that physicians should receive more training to identify nonmedical users, to discuss the potential danger of the stimulants, and to educate their patients regarding the risks associated with misuse and the legal responsibility of drug diversion.

In clinical practice, identifying the source of misused stimulants may also serve as a useful indicator of the specific needs and vulnerabilities of the patients. For example, patients who report obtaining their misused stimulants illegally or from doctors appear to be an increased risk of other substance use disorders. Those who report obtaining their misused stimulants from a physician should be screened for depression, anxiety or other mental health problems.

Several limitations to this study and the NSDUH data should be noted. First, the NSDUH asks for the most recent source of misused stimulants, but not the most commonly used source. Second, Adderall, a commonly used stimulant, was not included in the list of stimulants specifically enquired about and was included in the "other stimulants." There is some evidence that this approach to ascertaining Adderall may have missed a large proportion of Adderall user (Kroutil et al., 2010). Third, given the cross-sectional nature of the NSDUH, causal-relationship cannot be established here. Thus, for example, it is not clear from these data whether mental health problems preceded or followed stimulant misuse. Fourth, all of the data were based on self-report, which is open to recall or social-desirability bias. However, the validity of these reports has been established in a previous study (Harrison, 2007). Fifth, the mental health variables (depression, anxiety) used here were based on clinician-diagnoses communicated to the participants, which is conditional to having had contact with a clinician. This factor may also, at least partly, explain the association of physician source with these mental health indicators. Finally, questions used by the NSDUH do not differentiate between those who obtained their stimulant from friends versus relatives, and the implications and correlates of these two sources may be different (Schepis and Krishnan-Sarin, 2009).

5. Conclusion

Despite these limitations, findings from this study suggest that different sources of misused stimulants are associated with different risk profiles and stimulant use involvement. Those who obtained their misused stimulant from a physician

source carry a greater burden of mental health problems, whereas there is a stronger correlation between criminal activities and obtaining stimulants from illegal sources. Both these groups tend to have more serious stimulant use problems than the group who obtained their stimulants from friends or relatives. The implications of these differences in the source of misused stimulants may inform future prevention and treatment campaigns.

Table 1. Different types of prescription stimulant sources of past-year nonmedical prescription stimulant users in a sample of the US population aged 12 and above (N= 4,945): data from 2006–2011 National Survey on Drug Use and Health.

Sources	**N**	**Weighted % (95% confidence interval)**
Friends/relatives source	3813	75.1(72.8,77.3)
Got the stimulants from a friend or relative for free	2480	52.5 (50.2,54.9)
Bought the stimulants from a friend or relative	1044	7.5 (15.9,19.3)
Took the stimulants from a friend or relative without asking	289	5.0 (4.1,6.2)
Physician source	475	11.2(9.8,12.6)
Got one or more prescriptions for stimulants from just one doctor	427	10.3 (9.0,11.8)
Got prescriptions for stimulants from more than one doctor	48	2.9 (0.6,1.5)
Illegal source	485	9.8(8.1,11.5)
Wrote fake prescriptions for stimulants	20	0.5 (0.2,1.2)
Stole the stimulants from a doctor's office, clinic, hospital, or pharmacy	38	0.9 (0.5,1.6)
Bought the stimulants from a drug dealer or other stranger	363	6.7 (5.5,8.0)
Bought the stimulants on the Internet	64	1.8 (1.2,2.6)
Other source	172	3.9 (2.9,5.3)
Got the stimulants in some other way	172	3.9 (2.9,5.3)

Table 2. Characteristics of past-year nonmedical ADHD stimulant based on source of misused stimulants in a sample of the US population aged 12 and above (N= 4,773): data from 2006–2011 National Survey on Drug Use and Health.

Characteristics	Friend/ Relative source (N=3,813)	Physician source (N=475)	Physician source vs Friend/Relative source	Illegal source (N=485)	Illegal source vs Friend/Relative source
	N (Wgt%)	N (Wgt%)	OR (95% CI)	N (Wgt%)	OR (95% CI)
Sex					
Male	1792(49.0)	220(46.7)	1.00	281(58.3)	1.00
Female	2021(51.0)	255(53.3)	1.01(0.67,1.50)	204(41.7)	0.48(0.32,0.72)‡
Age					
12-17	846(11.6)	135(13.3)	1.00	132(14.4)	1.00
18-25	2442(48.2)	245(33.2)	0.58(0.40,0.85)†	281(40.6)	0.60(0.44,0.82)†
≥ 26	525(40.3)	95(53.5)	1.17(0.73,1.89)	72(45.3)	0.84(0.45,1.56)
Race					
Non-Hispanic White	3103(83.2)	350(78.9)	1.00	389(83.1)	1.00
Minorities	710(16.8)	125(21.1)	1.05(0.64,1.73)	96(16.9)	1.04(0.62,1.74)
Marital status[a]					
Married	270(18.9)	52(27.5)	1.00	41(28.7)	1.00
No longer married	152(9.1)	27(20.4)	2.01(0.85,4.75)	28(14.5)	0.71(0.22,2.22)
Never married	2545(71.4)	261(52.1)	0.50(0.25,1.00)	284(56.8)	0.48(0.19,1.21)
Employment[a]					
Full/Partial	2054(72.2)	210(65.8)	1.00	227(63.0)	1.00
Unemployed	291(8.1)	43(9.2)	0.93(0.48,1.78)	54(18.4)	2.79(1.18,6.60)*
Not labor force	622(19.7)	87(25.1)	1.26(0.73,2.15)	72(18.6)	1.26(0.68,2.34)
Education[a]					
< high school	350(11.1)	50(14.3)	1.00	84(18.9)	1.00
High school	763(23.5)	94(26.9)	1.83(0.90,3.73)	115(26.5)	0.56(0.31,0.99)*
≥ College	1854(65.4)	196(58.8)	1.20(0.65,2.20)	154(54.6)	0.37(0.20,0.69)†
Income					
< $20,000	1260(28.8)	160(27.1)	1.00	125(23.3)	1.00
$20,000- $49,999	1107(30.6)	142(33.4)	1.07(0.67,1.73)	169(37.4)	1.73(0.92,3.19)
$50,000- $74,999	508(13.2)	68(14.6)	1.35(0.72,2.53)	61(9.8)	1.02(0.63,1.65)
≥ $75,000	938(27.4)	105(24.9)	0.82(0.46,1.46)	130(29.6)	1.24(0.75,2.05)
Past-year Depression					
No	3128(86.4)	350(73.3)	1.00	361(78.1)	1.00
Yes	650(13.6)	110(26.7)	1.63(1.05,2.52)*	124(21.9)	1.28(0.80,2.07)
Past-year Anxiety					
No	3,362(89.1)	352(69.2)	1.00	411(86.2)	1.00
Yes	451(10.9)	123(30.8)	4.37(2.66,7.18)‡	74(13.8)	1.29(0.85,1.97)
Past-year mental health treatment					
No	2787(72.7)	262(51.3)	1.00	339(71.7)	1.00
Yes	1026(27.3)	213(48.7)	2.92(1.96,4.35)‡	146(28.3)	1.02(0.65,1.61)
Past-year SUD treatment	3413(90.3)	408(86.9)	1.00	381(81.4)	1.00
No	400(9.7)	67(13.1)	2.10(1.30,3.39)†	104(18.6)	2.50(1.49,4.18)†
Yes					

Past-year criminal behavior					
No	2370(89.1)	309(69.2)	1.00	204(53.4)	1.00
Yes	1443(10.9)	166(30.8)	1.07(0.67,1.70)	281(46.6)	2.62(1.67,4.10)‡
Past-year Incarceration					
No	3233(86.4)	398(87.3)	1.00	348(75.5)	1.00
Yes	580(13.6)	77(12.8)	1.09 (0.73,1.64)	137(24.5)	2.27(1.47,3.49)‡
Past-year alcohol dependence					
No	2950(78.3)	362(77.6)	1.00	361(78.4)	1.00
Yes	863(21.7)	113(22.4)	1.50(0.93,2.42)	124(21.6)	1.28(0.78,2.12)
Past-year drug dependence					
No	2796(76.9)	339(71.6)	1.00	279(65.0)	1.00
Yes	1017(23.1)	136(28.4)	1.73(1.15,2.61)†	206(35.0)	2.36(1.52,3.66)‡

*p<0.05, †p<0.01, ‡ p<0.001

a. Education, marital status, and employment status were examined in adults aged 18 and above only. Drug dependence did not include stimulant dependence.

Table 3. Onset, recency and severity of past-year nonmedical prescription stimulant use based on source of misused stimulants in a sample of the US population aged 12 and above (N= 4,773): data from 2006–2011 National Survey on Drug Use and Health.

	Early Onset (≤ age 13)		Past-month use		≥ 10 days in the past year		Past-year stimulant use disorder	
	Odds Ratio (95% CI)	Adjusted Odds ratio[a] (95% CI)	Odds ratio (95% CI)	Adjusted Odds ratio[a] (95% CI)	Odds ratio (95% CI)	Adjusted Odds ratio[a] (95% CI)	Odds ratio (95% CI)	Adjusted Odds ratio[a] (95% CI)
Physician source vs Friends/Relatives source	1.82(1.16,2.84)†	1.10(0.52,2.33)	3.25(2.39,4.41)‡	3.29(2.24,4.85)‡	3.10(2.09,4.60)‡	3.07(1.95,4.82)‡	2.88(1.82,4.58)‡	2.75(1.52,4.97)†
Illegal source vs Friends/Relatives source	2.36(1.41,3.95)†	2.07(1.02,4.15)*	1.66(1.12,2.47)*	1.55(1.00,2.40)*	2.36(1.58,3.54)‡	2.21(1.45,3.38)‡	2.80(1.93,4.06)‡	2.69(1.80,4.01)‡

*p<0.05, †p<0.01, ‡ p<0.001

[a.] Adjusted models were adjusted for sex, age race, education, marital status, employment, income, past-year major depression, anxiety disorder, criminal behaviors, and incarceration.

Chapter 4. Part A. Patterns of Concurrent Substance Use Among Adolescent Nonmedical ADHD Stimulant Users

Abstract

Objective: To identify subgroups of adolescents with nonmedical ADHD stimulant use according to patterns of concurrent problematic substance use.

Method: We used latent class analysis (LCA) to identify subgroups with concurrent problematic substance use (i.e. had any criteria of abuse or dependence) in a sample of 2,203 adolescent participants from the National Surveys on Drug Use and Health 2006-2011 who reported past-year nonmedical use of ADHD stimulants. Multivariate latent regression was used to assess the association of socio-demographic, mental health, deviant behavior, and service use characteristics with the latent classes.

Results: The best model fit was a four-class model, including a large class with frequent concurrent use of alcohol and marijuana (*Alcohol/Marijuana* class; 41.2%), a second large class with infrequent use of other substances (*Low substance* class, 36.3%), a third class characterized by more frequent misuse of prescription drugs (*Prescription drug* class; 14.8%), and finally a class characterized by problematic use of multiple substances (*Multiple substances* class; 7.7%). These four classes showed distinct socio-demographic and mental health profiles. Compared with individuals in *Low substance* class, those in the other three classes were all more likely to report mental health problems, deviant behaviors, mental and substance service use, with *Multiple substances* class being most likely to report social and behavioral problems.

Conclusions: Adolescent nonmedical ADHD stimulants users are a heterogeneous group with distinct classes with regard to mental health comorbidity, behavioral problems and service use. The findings have implications for planning a more tailored prevention and treatment programs based on their concurrent substance use in this age group.

1. Introduction

Nonmedical use of prescription stimulants, especially stimulants prescribed for treatment of Attention Deficit Hyperactivity Disorder (ADHD), has received increased research attention in the past decade (McCabe et al., 2007a; McCabe et al., 2007b; McCabe et al., 2005; Safer, 2000; Safer et al., 1996; Teter et al., 2005; Teter et al., 2006; White et al., 2006). These stimulants, including methylphenidate and mixed salts amphetamines, remain the first line of pharmacotherapy for ADHD (Olfson et al., 2003; Zito et al., 2003) and were classified as schedule II substances in the US Controlled Substances Act (CSA) due to their high abuse potential (Drug Enforcement Administration, 2003a).

Much of past research has focused on nonmedical prescription stimulant use among young adults (Arria et al., 2008; Garnier-Dykstra et al., 2012; Johnston, 2003; McCabe et al., 2009; McCabe et al., 2005; McCabe et al., 2007c; SAMHSA, 2009a; Teter et al., 2005; Teter et al., 2006; White et al., 2006. However, there is also evidence of a growing problem of nonmedical use among adolescents (Arria and Wish, 2006; Boyd et al., 2006, 2007; McCabe et al., 2007a; McCabe et al., 2004). According to data from the Monitoring The Future (MTF) survey, past-year nonmedical use of methylphenidate in high school seniors increased from 0.5% in 1995 to 2.5% in 2002 (Arria and Wish, 2006). A more recent report showed a continued growth between 2008 and 2013 found an increase from 6.8% to 8.7% in past-year nonmedical use and from 2.9% to 4.1% in current use of amphetamines in 12^{th} graders in this time period (Wadley, 2013). In a high school survey, 4.5% of students reported using prescription stimulants nonmedically, with 23.3% reporting

being approached to sell, give, or trade these drugs (McCabe et al., 2004). Emergency room visits involving ADHD stimulants tripled in the period between 2005 and 2010 highlighting the health burden of nonmedical use of these medications (SAMHSA, 2013b).

There is also growing evidence that nonmedical ADHD stimulant users are more likely to use other substances or to engage in risky behaviors (Boyd et al., 2006; McCabe et al., 2007a; McCabe et al., 2006a; McCabe et al., 2004; SAMHSA, 2009a). Among high school students, nonmedical prescription stimulant users reported significantly higher rates of alcohol and other drug use than nonusers (McCabe et al., 2004). Based on a report using the National Survey on Drug Use and Health (NSDUH), 90 percent of college students who had past-year nonmedical Adderall use also reported past-month binge drinking, more than half being heavy drinkers (SAMHSA, 2009a). In another survey conducted in 119 colleges in the United States, nonmedical prescription stimulant users were more likely to report use of alcohol, cigarettes, marijuana, ecstasy, cocaine and engaging in other risky behaviors (McCabe et al., 2005). Concurrent use of substances has been generally shown to be associated with worse psychological and social consequences in young adults (Barrett et al., 2006; Grant and Harford, 1990; Hedden et al., 2009). However, relatively little is known regarding the concurrent substance use patterns among adolescent who use prescription stimulants nonmedically (Barrett et al., 2006; Grant and Harford, 1990; Hedden et al., 2009). In particular, it is not clear whether concurrent use of other substances is common among all nonmedical users of stimulants, or simply exists in certain subgroups. Identifying subgroups of ADHD

stimulant users based on concurrent substance use has implications for the study of the epidemiology of nonmedical stimulant use, which can help to identify youth who are at particularly high risk of other substance use.

In this study, we used data from national surveys of general population adolescents who use stimulants nonmedically to explore subgroups according to concurrent problematic substance use patterns, including alcohol and illegal drugs, using latent class analysis. We further examined variations in socio-demographic characteristics, mental health profiles, deviant behaviors, and service use among the empirically identified classes. We hypothesized that there exist at least 2 subgroups of nonmedical stimulant users, one with lower prevalence of other substance use who may be using stimulants for improving attention and concentration and, perhaps as a study aid, and uses few other substances, and another group who abuses these drugs recreationally and is likely to use other substances concurrently.

2. Methods

2.1. Study sample and measures

Combined annual data from the NSDUH public use data files for the years 2006 to 2011 (N= 338,495) were analyzed. The study sample was restricted to adult participants aged 12 to 17 (N=109,466) who reported using ADHD medications nonmedically in the past year (N=2,203). The NSDUH is an annual cross-sectional survey sponsored by the Substance Abuse and Mental Health Administration (SAMHSA) and is designed to provide estimates of the prevalence of alcohol and drug use in the household population of the United States, 12 years of age and older.

The survey employs a 50-state design with an independent multistage area probability sample for each of the 50 states and the District of Columbia. African-Americans, Hispanics, and youth are over-sampled to increase the precision of estimates for these groups. The response rate for household screening ranged from 87% to 91% and for completed interviews from 74% to 76% across the 6 years.

Survey items were administered by computer-assisted personal interviewing (CAPI) conducted by an interviewer and audio computer-assisted self-interviewing (ACASI) for sensitive questions. Use of ACASI was designed to provide participants with a highly private and confidential means of responding to questions and to increase the validity of reporting of illegal drug use and other sensitive behaviors. Participants were offered a $30 incentive payment for participation in the survey. Detailed information about the sampling and survey methodology of the NSDUH are found elsewhere (SAMHSA, 2007, 2008, 2009, 2010, 2011, 2012).

2.2. Assessments

2.2.1. Assessment of past-year nonmedical ADHD stimulant use

For the current analyses, ADHD stimulants were defined as stimulants with specific indications for treatment of ADHD, and included Ritalin® or methylphenidate, Cylert®, Dexedrine®, Dextroamphetamine, Adderall®, and Vyvanse®. The survey used the following question to assess nonmedical use of any ADHD stimulants in the lifetime: “Have you ever, even once, used [Drug name] that was not prescribed for you or that you took only for the experience or feeling it caused?” Nonmedical ADHD stimulant use was defined as past-year if their time since last use was within the prior 12 months.

2.2.2. Assessment of socio-demographic characteristics

Socio-demographic variables included in the analyses were sex, age (12-13, 14-15, 16-17), race/ethnicity (non-Hispanic white, racial/ethnic minority), school dropout, average grade (C and above, D or lower) in the last period completed, and annual household income (≤ $19,999, $20,000-$34,999, $35,000-$69,999, ≥ $70,000).

2.2.3. Assessment of past-year problematic substances use

Past-year problematic substance use was defined by fulfilling any of the criteria for past-year substance abuse or dependence based on the Diagnostic and Statistical Manual of Mental Disorders –IV (DSM-IV) (American Psychiatric Association, 1994). The substances examined included alcohol, marijuana, cocaine, heroin, hallucinogens, inhalants, prescription opioids, and tranquilizers/sedatives (combined). Participants who endorsed any criteria of abuse or dependence for these substances and specified their recent use in the past 12 months were categorized as past-year problematic users.

2.2.4. Assessment of past-year mental health and deviant behavior variables

Mental health variables included were past-year anxiety disorder and major depressive disorder (MDD), as ascertained by participants' self-report of past-year diagnosis by a medical doctor or health care professional. Past-year mental health and substance abuse service use were ascertained by asking participants whether they received any mental health treatment or substance abuse treatment in the past year. Past-year deviant behaviors were assessed by asking the participants how many times they had attacked someone with the intent to seriously hurting them, how many times

they had sold illegal drugs, and how many times they had stolen or tried to steal anything worth more than $50 in that time frame. Consistent with past research (Martins et al., 2006; Martins et al., 2009), participants who reported any of the four behaviors were categorized as having "deviant behaviors" (0 for none of these behaviors and 1 for engaging in one of more of these behaviors at least once). Past-year incarceration was assessed by asking participants how many times in the past 12 months they had been arrested and charged with breaking the law without counting minor traffic violations (0 for none and 1 for at least once). Past-year sexually transmitted disease (STD) was also assessed by participant self-reports of diagnosis by a medical doctor or health care professional.

2.3. Statistical analyses

Complex latent class analysis (LCA) was used to identify subgroups according to concurrent problematic substance use among individuals who used ADHD stimulants nonmedically in the past year. We performed LCA for 1 to 6 classes in order to ascertain the model with the optimal fit. Minimum values of the Bayesian Information Criterion (BIC) was given priority over other fit statistics such as Akaikes Information Criterion (AIC) and Sample Size Adjusted BIC (ABIC), given its more stable performance in simulation studies (Nylund et al., 2007). We also considered the class size and clinical interpretability in selecting the model.

LCA was applied using the Mplus software (Muthén, 1998-2010). We chose eight dichotomous substance use variables (past-year problematic use of alcohol, marijuana, cocaine, heroin, hallucinogens, inhalants, prescription opioids, and

tranquilizers/sedatives) to empirically determine the smallest number of classes with similar drug use patterns that explain the response pattern in the data.

Once the number of classes was ascertained, correlates including socio-demographics, mental health and deviant behaviors were incorporated into the models using unadjusted and adjusted multinomial regression models. These analyses were conducted using a modal assignment latent regression approach with Stata 13.0 software (StataCorp, 2013). All analyses included adjustment for the complex survey design by taking into account the survey weights, clustering and stratification. All the percentages reported are weighted. A $p<0.05$ was used to ascertain the statistical significance of findings.

3. Results

3.1. Characteristics of the nonmedical ADHD stimulant users

The frequency distribution of participant characteristics is presented in Table 1. Approximately 3.2% (n = 2,203) of adolescent participants from the NSDUH reported nonmedical use of ADHD stimulants in the past year. A relatively higher percent of nonmedical ADHD stimulant use was found among females (51.8%), aged 16-17 (64.2%), whites (80.7%), and with a household income < $20,000 (39.9%). Our adjusted logistic regression analyses further showed that they were more likely to be female (adjusted odds ratio, aOR=1.46, 95%CI [1.30,1.65]), aged 16-17 versus aged 12-13 (aOR=6.93,[5.45,8.81]), white versus in minority (aOR=0.29,[0.24,0.36]), to have grade D or lower (aOR=1.35,[1.07,1.70]), to come from family with household income ≥ $75,000 (aOR=1.40,[1.11,1.77]). They were

also more likely to report depression (aOR=1.60, [1.31,1.95]), anxiety disorder (aOR=1.31, [1.00,1.71]), to have received mental health treatment (aOR=1.38, [1.19,1.60]) and SUD treatment (aOR=2.90, [2.30, 3.66]), to report deviant behaviors (aOR=6.60, [5.69,7.66]), incarceration (aOR=2.03, [1.65,2.50]), and sexually transmitted disease (aOR=1.63,[1.06,2.50]) in the past year.

3.2. Subtypes of nonmedical ADHD stimulant users by LCA

The most commonly used substance among nonmedical ADHD stimulant users was alcohol (53.3%), followed by marijuana (47.9%), pain relievers (23.4%), hallucinogens (12.4%), tranquilizers and sedatives (9.9%), cocaine (7.3%), inhalants (5.8%) and heroin (1.7%).

Latent class analysis was performed for 1 to 7 class models. The fit statistics of BIC was lowest for the 4-class model and the AIC and ABIC for the 4 class model were similar to the 5-class model (Appendix 2), suggesting that the minimum fit index values were obtained for the 4-class model.(Nylund et al., 2007). By taking into account the minimum value of BIC as well as the clinical interpretability, a 4-class model was selected. Fit statistics were shown in Appendix Table 2.

Figure 1 presents prevalence of problematic use of different substances in the four classes of nonmedical ADHD stimulant users. Class 1 constituted 36.3% of the sample was comprised of individuals with low probabilities of problematic use of alcohol and prescription opioids and near zero probabilities of other problematic substance use (*Low substance* class). Class 2 made up 14.8% of the study sample and included individuals with moderate probabilities of problematic use of alcohol and marijuana, but additionally included participants with high probabilities of

problematic use of pain relievers and sedatives/tranquilizers (*Prescription drug* class). Class 3 included individuals with remarkably high probabilities of problematic use of marijuana and alcohol and was the largest class (*Alcohol/marijuana* class, 41.2%). Finally, class 4 was comprised of individuals who had the highest probabilities of problematic use of most of the substances examined (*Multiple substance class*, 7.7%).

3.3. *Characteristic of participants in the LCA-defined classes*

Table 2 presents the socio-demographic, mental health, service use and deviant behavior profiles of the 4 classes of past-year nonmedical ADHD stimulant users. *Prescription drug, Alcohol/marijuana*, and *Multiple substance* classes showed particularly high prevalence of deviant behaviors (*Prescription drug*: 64.8%; *Alcohol/marijuana*: 60.3%; *Multiple substance*: 85.5%) and incarceration (*Prescription drug*: 26.3%; *Alcohol/marijuana*: 23.6%; *Multiple substance*: 34.2%). Furthermore, 46.4% of those in *Prescription drug* class reported past-year mental health service use and 27.1% reported a depression diagnosis.

Results from the unadjusted and adjusted latent regression models comparing participants in the latent classes with those in *Low substance* class as the reference category are presented in Table 3. Compared to the *Low substance* class, participants in the *Prescription drug* class were more likely to be female (aOR=1.56, [1.17,2.10]). Participants in the *Alcohol/marijuana* and *Multiple substance* classes were more likely to be in the 16-17 years age group vs. the 12-13 year group. Furthermore, all these three classes were significantly more likely than the *Low substance* class to

have average grades of D or lower. *Multiple substance* class was more likely to report school dropouts (aOR=2.62, [1.29,5.34]).

Relative to the Low substance class, the other three classes were associated with higher odds of clinician-identified depression, mental health and substance service use, deviant behaviors and incarceration. *Prescription drug* and *Multiple substance* class were additionally associated with higher odds of clinician-identified anxiety disorder. *Multiple substance* class showed particularly higher odds of substance treatment, deviant behaviors and incarceration.

4. Discussion

The present study found that approximately 3.2% of adolescents aged 12-17 in the general household population reported past-year nonmedical use of prescription stimulants. Among them, more than half reported concurrent problematic substance use with the most frequently used being alcohol (53.3% of nonmedical ADHD stimulant users), marijuana (47.9%) and pain relievers (23.4%). Furthermore, this study found that with regard to concurrent problematic substance use, nonmedical ADHD stimulant users are a heterogeneous group which encompasses four classes with distinct psychiatric and social profiles, which has value for risk evaluation and preventive strategy development.

The classes that we labeled as *Prescription drug*, *Alcohol/marijuana* and *Multiple substance* classes were all more likely to report mental health problems, mental health and substance service use, and deviant behaviors compared to the *Low substance* class, which had the lowest prevalence of concurrent problematic

substance use. Previous studies have found relationships between nonmedical use of prescription stimulants and presence of depressed mood among youth (Compton et al., 2006; Poulin, 2007; Teter et al., 2010). Our study further points out that the association with mood disorders may be more pronounced in the subgroups that report more concurrent problematic substance use. Considering individuals with co-occurring mental and substance disorders have been found to have higher rate of service use than those without co-occurring disorders (Chen et al., 2013; Wang et al., 2005), higher prevalence of mental and substance service use was also observed in the three classes. Our finding underscores the significance of screening for mental problems among the nonmedical ADHD stimulant users.

The findings of greater deviant behaviors and poorer academic performance among the three classes which used more substances are particularly noteworthy. Consistent with previous reports in college students, we found nonmedical prescription stimulant users with poorer academic performances among adolescents, which broke the myth that prescription stimulants work well as a study aid (Arria, 2008; Garnier-Dykstra et al., 2012; McCabe et al., 2004). The underlying reasons for decreased academic performance remains uncertain (Arria and DuPont, 2010), this study provides evidence that involvement in more problematic substance use may contribute to this phenomenon despite that temporal relationship could be not established. The motives for stimulant use may also vary considerably among stimulant users with and without concurrent other substance use (McCabe and Cranford, 2012). These differences call for a more nuanced approach to prevention

and treatment of adolescents with nonmedical stimulant use based on concurrent use of other substances and motives for their stimulant use.

Despite the similarities among the three classes with higher prevalence of concurrent substance use problems with regard to psychiatric and behavior profiles, these three classes showed some differences in socio-demographic profiles. Most notably, participants in the *Prescription drug class*, consisting of 14.8% of our study population, were more likely to be female compared to the *Low substance use* class, while the other two classes did not show such gender differences. This finding is consistent with past research which has found that females are at increased risk for nonmedical opioid and tranquilizers use (Roe et al., 2002; Simoni-Wastila, 2000).

Compared to the *Low substance* class, the *Multiple substance* class had exceptional higher odds of reporting mental health problems, mental and substance service use and behavior problems. Comorbid substance use and psychiatric disorders confer an additional risk for not only worse social outcomes but also and poorer treatment response (Cuffel et al., 1994; Grella et al., 2001; Hasin et al., 2007b; Strain, 2002a). Similarly, concurrent use of multiple substances is linked to more physical consequences and criminal involvement (Hasin et al., 2007b; Hedden et al., 2009). Considering the fact that adolescents in this class were also more likely to drop out of school, prevention efforts targeted to adolescents at risk of dropping out of schools might improve the psychiatric, social, and health outcomes of this population.

This study has multiple strengths, including a large sample size and generalizability to the US household population. However, the result should be

interpreted with caution due to the limitations of the study and of the NSDUH data. First, all the information were based on self-report, which is prone to recall and other reporting biases, although the validity of substance use reports in NSDUH has been established previously (Harrison, 2007). Second, the cross-sectional survey data limits assessment of temporal relationships and causal inferences. Third, we used clinician-identified depression and anxiety in this study, which are subject to health service access and availability. Lastly, the information regarding the frequency of nonmedical prescription stimulant use was not available, thus whether these subgroups differ by their level of severity remains unknown.

5. Conclusion

Our results suggest that adolescents who use ADHD stimulants nonmedically are not a homogeneous group. Rather, they comprise subgroups with distinct profiles with regard to concurrent substance use, socio-demographic characteristics, academic performance and mental health profiles. Elucidating concurrent substance use patterns among adolescent stimulant users is crucial for identifying these subgroups and addressing their special needs. Adolescence underscores a critical period to develop substance use disorders (Kandel and Logan, 1984; Kosterman et al., 2000); thus strategies to curb nonmedical stimulant use and to further avoid other substance involvement are exigent.

Table 1. Characteristics of past-year nonmedical ADHD stimulant users in a sample of the US adolescents aged 12-17(n=109,466): data from 2006–2011 National Survey on Drug Use and Health.			
Characteristics	**Nonmedical ADHD stimulant use**		Comparison of groups aOR (95% CI)
	Reported (N=2,203)	Not reported (N=107,263)	
Gender			
Male	1,073(48.2)	54,855(51.2)	1.00
Female	1,130(51.8)	52,808(48.9)	1.46(1.30,1.65)‡
Age			
12-13	141(7.0)	34,260(32.1)	1.00
14-15	616(28.8)	36,269(34.2)	3.44(2.56,4.61)‡
16-17	1,446(64.2)	36,734(33.7)	6.93(5.45,8.81)‡
Race			
Non-Hispanic White	1,727(80.7)	63,194(58.0)	1.00
Minorities	76(19.3)	44,069(42.0)	0.29(0.24,0.36)‡
School dropout			
No	2,088(95.0)	105,890(98.9)	1.00
Yes	115(5.0)	1,366(1.1)	1.49(0.90,2.46)
Average Grade			
A,B, and C	1,747(86.0)	89,970(94.9)	1.00
D or lower	316(14.0)	5,770(5.1)	1.35(1.07,1.70)*
Income			
< $20,000	310(13.3)	18,423(16.8)	1.00
$20,000- $49,999	734(31.4)	34,737(31.4)	1.30(1.05,1.61)*
$50,000- $74,999	384(15.4)	20,236(18.0)	1.13(0.86,1.47)
≥ $75,000	775(39.9)	33,867(34.0)	1.40(1.11,1.77)†
Past-year depression			
No	1,747(84.5)	99,590(97.0)	1.00
Yes	351(15.5)	3,404(3.0)	1.60(1.31,1.95)‡
Past-year anxiety			
No	1,999(91.5)	105,302(98.3)	1.00
Yes	204(8.6)	1,961(1.7)	1.31(1.00,1.71)*
Past-year mental health treatment			
No	1,518(71.2)	92,434(87.7)	1.00
Yes	649(28.8)	13,600(12.3)	1.38(1.19,1.60)‡
Past-year SUD treatment			
No	1,908(87.1)	105,993(98.9)	1.00
Yes	295(12.9)	1,270(1.1)	2.90(2.30,3.66)‡
Past-year deviant behavior	1,053(49.3)	95,534(89.5)	1.00
No	1,150(50.7)	11,729(10.5)	6.60(5.69,7.66)‡
Yes			
Past-year incarceration			
No	1,756(81.1)	103,604(97.0)	1.00
Yes	446(18.9)	3,650(3.0)	2.03(1.65,2.50)‡
Past-year STD			
No	2,157(98.1)	106,873(99.7)	1.00
Yes	46(1.9)	390(0.3)	1.63(1.06,2.50)*

*p<0.05, †p<0.01, ‡ p<0.001

a. Adjusted model was adjusted for all variables included in this model.

Table 2. Characteristics of past-year nonmedical ADHD stimulant users, by concurrent problematic substance use class in a sample of the US population aged 12-17 (N= 2,203): data from 2006–2011 National Survey on Drug Use and Health.

Characteristics, N (Wgt%)	**Low substance class (n=784)**	**Prescription drug class (n=343)**	**Alcohol/ marijuana class (n=896)**	**Multiple substance class (n=180)**
Gender				
Male	376 (48.0)	136 (38.1)	474 (52.3)	87 (46.5)
Female	408 (52.0)	207 (61.9)	422 (47.7)	93 (53.5)
Age				
12-13	87 (11.1)	26 (11.4)	17 (2.3)	11 (4.4)
14-15	226 (19.9)	121 (32.3)	225 (27.0)	44 (67.1)
16-17	471 (59.0)	196(56.4)	654 (70.7)	125 (68.5)
Race				
Non-Hispanic White	595 (77.6)	265 (79.5)	725 (83.3)	142 (83.4)
Minorities	189 (22.4)	78 (20.5)	171 (16.7)	38 (16.6)
School Dropout				
No	765 (97.5)	324 (95.3)	837 (93.7)	162 (89.5)
Yes	19 (2.6)	19 (4.7)	59 (6.3)	18 (10.5)
Average Grade				
A,B, and C	713 (91.2)	273 (81.1)	759 (86.2)	142 (81.8)
D or lower	71 (8.8)	70 (18.9)	137 (13.8)	38 (18.2)
Household Income				
< $20,000	103 (12.4)	69 (19.6)	105 (10.8)	33 (18.9)
$20,000- $49,999	233 (28.1)	111 (33.6)	331 (34.4)	59 (26.6)
$50,000- $74,999	140 (15.8)	66 (16.0)	152 (15.7)	26 (11.1)
≥ $75,000	308 (43.8)	97 (30.8)	308 (39.2)	62 (43.4)
Past-year depression				
No	667 (91.9)	237 (72.9)	723 (85.0)	120 (68.5)
Yes	72 (8.1)	86 (27.1)	140 (15.0)	53 (31.5)
Past-year anxiety				
No	739 (95.0)	291 (86.8)	825 (93.0)	144 (75.6)
Yes	45 (5.0)	52 (13.2)	71 (7.0)	36 (24.4)
Past-year mental health treatment				
No	601 (78.6)	178 (53.6)	646 (72.9)	93 (61.3)
Yes	166 (21.4)	157 (46.4)	241 (27.1)	85 (38.7)
Past-year SUD treatment				
No	754 (96.8)	270 (79.3)	769 (85.9)	115 (62.2)
Yes	30 (3.3)	73 (20.7)	127 (14.1)	65 (37.8)
Past-year deviant behaviors				
No	572 (73.3)	101 (35.2)	355 (39.7)	25 (14.2)
Yes	212 (26.7)	242 (64.8)	541 (60.3)	155 (85.8)
Past-year incarceration				
No	718 (92.7)	239 (73.7)	686 (76.4)	113 (65.8)
Yes	66 (7.3)	104 (26.3)	210 (23.6)	66 (34.2)
Past-year STD				
No	776 (98.9)	333 (97.4)	879 (98.0)	169 (95.5)
Yes	8 (1.1)	10 (2.6)	17 (2.0)	11 (4.5)

Table 3. Characteristics of past-year nonmedical ADHD stimulant users, by concurrent problematic substance use class in a sample of the US population aged 12-17 (N= 2,203): data from 2006–2011 National Survey on Drug Use and Health.

Characteristics	**Prescription drug class vs. Low substance class**		**Alcohol/marijuana class vs. Low substance class**		**Multiple substance class vs. Low substance class**	
	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)
Gender						
Male	1.00	1.00	1.00	1.00	1.00	1.00
Female	1.50(1.10,2.04)*	1.56(1.17,2.10)†	0.84(0.66,1.08)	0.84(0.66,1.08)	1.06(0.68,1.66)	1.08(0.66,1.75)
Age						
12-13	1.00	1.00	1.00	1.00	1.00	1.00
14-15	1.06(0.57,1.95)	1.32(0.67,2.58)	4.41(1.73,11.26)‡	3.64(1.44,9.19)†	2.31(1.19,4.48)*	2.19(1.02,4.70)*
16-17	0.94(0.53,1.65)	1.28(0.66,2.45)	5.86(2.49,13.78)‡	4.89(2.11,11.30)‡	2.95(1.50,5.83)†	2.42(1.14,5.18)*
Race						
Non-Hispanic White	1.00	1.00	1.00	1.00	1.00	1.00
Minorities	0.90(0.61,1.32)	0.69(0.45,1.07)	0.69(0.51,0.94)*	0.75(0.56,1.01)	0.69(0.40,1.21)	0.76(0.43,1.36)
School dropout						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	1.87(0.79,4.46)	1.50(0.63,3.53)	2.57(1.32,5.00)†	1.60(0.84,3.02)	4.49(1.88,10.73)†	3.25(1.08,9.83)*
Average Grade						
A,B, and C	1.00	1.00	1.00	1.00	1.00	1.00
D or lower	2.50(1.51,4.13)†	2.33(1.38,3.94)†	1.67(1.18,2.37)†	1.82(1.25,2.67)†	2.46(1.29,4.69)†	2.62(1.29,5.34)†
Household Income						
< $20,000	1.00	1.00	1.00	1.00	1.00	1.00
$20,000- $49,999	0.75(0.46,1.24)	0.71(0.43,1.18)	1.40(0.91,2.13)	1.31(0.90,1.91)	0.62(0.30,1.29)	0.62(0.30,1.24)
$50,000- $74,999	0.64(0.33,1.21)	0.62(0.33,1.16)	1.13(0.68,1.88)	0.98(0.57,1.68)	0.46(0.24,0.90)*	0.49(0.25,0.99)*
≥ $75,000	0.44(0.27,0.72)†	0.45(0.28,0.73)*	1.02(0.65,1.59)	0.90(0.57,1.41)	0.64(0.33,1.29)	0.68(0.33,1.41)
Past-year depression						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	4.24(2.72,6.60)‡	3.54(2.23,5.61)‡	2.01(1.34,3.04)†	1.98(1.30,3.02)†	5.24(2.95,9.20)‡	5.54(3.10,8.90)‡
Past-year anxiety						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	2.86(1.53,5.36)‡	2.16(1.08,4.32)*	1.43(0.77,2.65)	1.32(0.71,2.41)	6.11(3.27,11.42)‡	4.47(2.35,8.53)‡
Past-year mental health treatment						
No	1.00	1.00	1.00	1.00	1.00	1.00

Yes	3.18(2.20,4.60)‡	2.81(1.88,4.22)‡	1.36(1.02,1.83)*	1.49(1.12,1.98)†	2.32(1.52,3.53)‡	2.80(1.77,4.11)‡
Past-year SUD treatment	1.00	1.00	1.00	1.00	1.00	1.00
No	7.78(4.72,12.82)‡	6.56(3.83,11.22)‡	4.87(2.79,8.53)‡	4.16(2.29,7.57)‡	18.08(10.06,32.50)‡	17.17(9.37,31.49)‡
Yes						
Past-year deviant behaviors	1.00	1.00	1.00	1.00	1.00	1.00
No	5.04(3.38,7.50)‡	5.55(3.60,8.56)‡	4.16(3.25,5.33)‡	4.07(3.17,5.22)‡	16.51(10.33,26.39)‡	15.21(9.11,25.37)‡
Yes						
Past-year incarceration						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	4.57(2.97,7.17)‡	3.89(2.37,6.39)‡	3.95 (2.69,5.80)‡	3.28(2.22,4.87)‡	6.64(4.18,10.52)‡	6.28(3.65,10.82)‡
Past-year STD						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	2.53(0.71,8.97)	1.86(0.45,7.72)	1.86(0.48,7.32)	1.64(0.36,7.42)	4.35(1.14,16.63)*	3.33(0.67,16.57)

*p<0.05, †p<0.01, ‡ p<0.001

a. Adjusted model was adjusted for gender, age, race, school dropout, grades, and income for these variables. For mental health and deviant behaviors variables, adjusted model was adjusted for gender, age, race, school dropout, average grades, household income, and the measured variable itself.

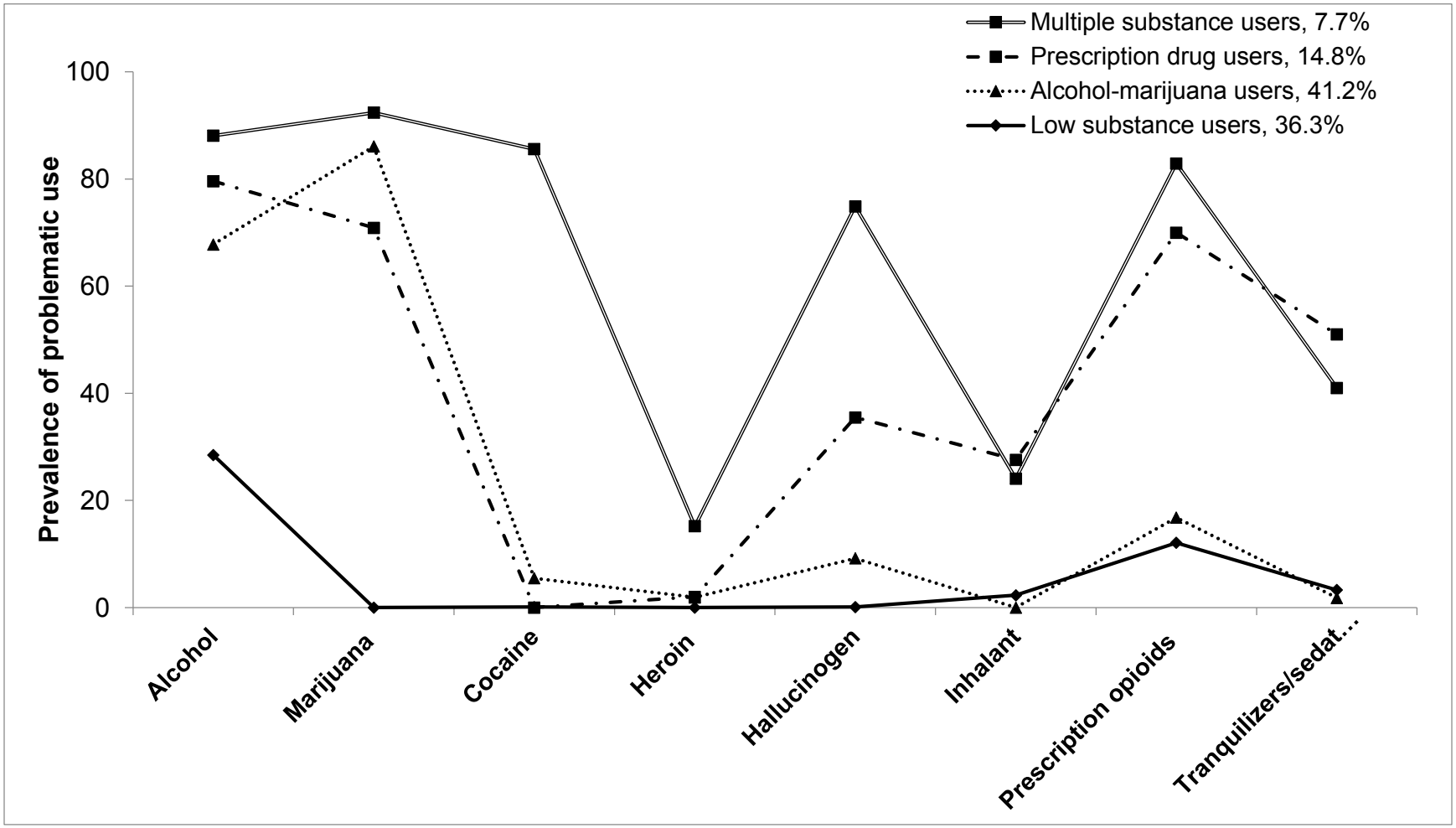

Figure 1. Prevalence of problematic use of other substances in four classes of adolescents with past-year nonmedical ADHD stimulant use in the 2006–2011 National Survey on Drug Use and Health.

Chapter 4. Part B. Patterns of Concurrent Substance Use Among Adult Nonmedical ADHD Stimulant Users

Abstract

Aims: To examine patterns of concurrent substance use among adults with nonmedical ADHD stimulant use.

Methods: We used latent class analysis (LCA) to examine patterns of past-year problematic substance use (met any criteria for abuse or dependence) in a sample of 6,103 adult participants from the National Surveys on Drug Use and Health 2006-2011 who reported past-year nonmedical use of ADHD stimulants. Multivariate latent regression was used to assess the association of socio-demographic, mental health and deviant behavior characteristics with the latent classes.

Results: A four-class model had the best model fit: 1) a class of participants with low probabilities for any problematic substance use (*Low substance class*, 53.3%); 2) problematic users of all types of prescription drugs (*Prescription drug class*, 13.3%); 3) participants with high probabilities of problematic alcohol and marijuana use (*Alcohol/Marijuana class*, 28.8%); and 4) those with high probabilities of problematic use involving multiple drugs and alcohol (*Multiple substance class*, 4.6%). Regression analyses indicated that a) participants in the 4 classes had distinct socio-demographic, mental health and service use profiles; b) individuals in the Multiple substance class were more likely to report mental health problems, deviant behaviors, and service use.

Conclusion: Nonmedical users of prescription stimulants are a heterogeneous group with a large subgroup rarely having any problematic use of other substances. These

subgroups have distinct patterns of mental health comorbidity, behavior problems and service use, with implications for prevention and treatment of nonmedical stimulant use.

1. Introduction

Nonmedical use of prescription stimulants, especially stimulants commonly prescribed for treatment of ADHD, has received increased research attention in the past decade (McCabe et al., 2007a; McCabe et al., 2007b; McCabe et al., 2005; Safer, 2000; Safer et al., 1996; Teter et al., 2005; Teter et al., 2006; White et al., 2006). These Attention Deficit Hyperactivity Disorder (ADHD) stimulants mainly include methylphenidate and mixed amphetamine salts (Olfson et al., 2003; Zito et al., 2003), both of which are classified as schedule II based on the Controlled Substances Act (CSA), indicating their high abuse potential (Drug Enforcement Administration, 2003a).

Several U.S. epidemiological surveys have shown that nonmedical ADHD stimulant use is a growing problem especially among young adults (Johnston, 2003a; SAMHSA, 2009a). A Web survey using an undergraduate sample in the Midwest U.S. showed that 8.1% of participants reported lifetime nonmedical ADHD stimulants use and 5.4% reported nonmedical use in the prior year (Vetter et al., 2008). Other college based studies have had similar results with lifetime prevalence as high as 6.9% to 8.3% and past-year prevalence ranging from 4.1% to 5.9% (McCabe et al., 2005; Teter et al., 2006). Interestingly, college enrollment is a prominent risk factor for ADHD stimulant misuse. Data from the Monitoring the Future (MTF) study and the National Survey on Drug Use and Health (NSDUH) have shown that college students are twice as likely to report nonmedical use of ADHD stimulants compared to their counterparts not attending college (Johnston, 2003a; SAMHSA, 2009a). Most previous studies focus on young adults (McCabe et

al., 2006a; McCabe et al., 2005; SAMHSA, 2009a; Teter et al., 2005; Teter et al., 2006; White et al., 2006), thus failing to offer a complete picture of users in the general population.

Past research also provides compelling evidence that nonmedical use of ADHD stimulants is associated with high risk behaviors such as other substance use or deviant behaviors (McCabe, 2008; McCabe et al., 2005; SAMHSA, 2009a; Teter et al., 2005). A report based on the College Alcohol Study (CAS) showed that nonmedical ADHD stimulants users were 10 times more likely than their counterpart to report past-year marijuana use, 7 times more likely to report binge drinking, 20 times for cocaine use, and 5 times for drunken driving (McCabe et al., 2005). Another self-administrative web survey in college-age youth also reported that nonmedical ADHD stimulants use was associated with higher occurrence of substance use, regardless of their motivation (Teter et al., 2005). Based on a NSDUH report, 90 percent of college students who used Adderall® nonmedically reported past-month binge drinking, and more than half of them were heavy alcohol users (SAMHSA, 2009a). Another study using NSDUH data further revealed that nonmedical ADHD stimulants use was usually preceded by other illegal substance use (Sweeney et al., 2013).

While prior research indicates that nonmedical ADHD stimulant users have greater concurrent drug use or risky behaviors when compared with non-users (McCabe et al., 2007a; McCabe et al., 2005; McCabe and Teter, 2007; SAMHSA, 2009a; Teter et al., 2005; Teter et al., 2006; White et al., 2006), it is unclear whether distinct subgroups of nonmedical ADHD stimulant users can be identified based on

their concurrent drug use patterns. Past research suggests that the motives for nonmedical ADHD stimulant use are varied, ranging from cognitive enhancement and scholastic study aid to recreational use, suggesting the heterogeneity of this population (Teter et al., 2005; White et al., 2006). It is therefore important to know whether or not these variations are reflected in the patterns of concurrent substance use. The delineation of these subgroups has implications for prevention and treatment of non-medical users of stimulants as concurrent use of substances are associated with more significant physical and psychological consequences compared to single substance use (Conway et al., 2003; Kandel et al., 2001; Tittle et al., 2003). For example, concurrent alcohol and cocaine users have a higher odds for the occurrence of past-year sexually transmitted diseases (STDs) and incarceration relative to single drug users (Hedden et al., 2009).

In this study, we aimed to first identify the heterogeneous subgroups among nonmedical ADHD stimulant users by examining their concurrent problematic substance use patterns (defined as having any criteria for abuse or dependence), including alcohol and illegal drugs, using latent class analysis. Second, we examined the socio-demographic, psychological and social characteristics of these subgroups. We hypothesized that the class of nonmedical ADHD stimulant users with greater concurrent problematic substance use (i.e. high probabilities of multiple types of problematic substance use) would have more severe psychological problems, a greater number of deviant behaviors, and poorer social outcomes.

2. Methods

2.1. Study sample and measures

Combined annual data from the NSDUH public use data files for the years 2006 to 2011 (N= 338,495) were analyzed. The study sample was restricted to adult participants aged 18 or older (N=229,029) who reported using ADHD medications nonmedically in the past year (N=6,103). The NSDUH is an annual cross-sectional survey sponsored by the Substance Abuse and Mental Health Administration (SAMHSA) and is designed to provide estimates of the prevalence of alcohol and drug use in the household population of the United States, 12 years of age and older. The survey employs a 50-state design with an independent multistage area probability sample for each of the 50 states and the District of Columbia. African-American, Hispanic, and young populations are over-sampled to increase the precision of estimates for these groups. The response rate for household screening ranged from 87% to 91% and for completed interviews from 74% to 76% across the 6 years. Survey items were administered by computer-assisted personal interviewing (CAPI) conducted by an interviewer and audio computer-assisted self-interviewing (ACASI). Use of ACASI was designed to provide participants with a highly private and confidential means of responding to questions and to increase the validity of reporting of illegal drug use and other sensitive behaviors. Participants were offered a $30 incentive payment for participation in the survey. Detailed information about the sampling and survey methodology of the NSDUH are found elsewhere (SAMHSA, 2007, 2008, 2009, 2010, 2011, 2012).

2.1.1. Assessment of past-year nonmedical ADHD stimulant use

For the current analyses, ADHD stimulants are defined as stimulants with specific indications for treatment of ADHD, and included Ritalin® or methylphenidate, Cylert®, Dexedrine®, Dextroamphetamine, Adderall®, and Vyvanse®. The survey used the following question to assess nonmedical use of any ADHD stimulants in the lifetime: "Have you ever, even once, used [Drug name] that was not prescribed for you or that you took only for the experience or feeling it caused?" Nonmedical ADHD stimulant use was defined as past-year if their time since last use was within the prior 12 months.

2.1.2. Socio-demographic measures

Socio-demographic variables included in the analyses were gender, age (18-25, ≥ 26), race/ethnicity (non-Hispanic white, race/ethnic minority), marital status (married, no longer married, never married), employment status (partial or full employment, unemployed, not in the labor force), education (less than high school, high school, college and above), annual household income (≤ $19,999, $20,000-$34,999, $35,000-$69,999, ≥ $70,000).

2.1.3. Past-year problematic substances use measures

In order to reflect the spirit of DSM-5 (Harris and Edlund, 2005) that substance use disorders are dimensional instead of categorical disorders, we chose problematic substance use as the observed variables to identify the subgroups of nonmedical ADHD stimulant users. Past-year problematic substance use was defined by fulfilling any criteria for past-year substance abuse or dependence based on the Diagnostic and Statistical Manual of Mental Disorders–IV (DSM-IV) criteria (American Psychiatric Association, 1994). Substance abuse criteria included role

interference, hazardous use, problems with the law, and relationship problems. Substance dependence criteria included tolerance, withdrawal, taking larger amounts of substances or taking them for longer periods than intended, inability to cut down, time spent using the substance, giving up activities, and continued use despite substance-related problems in the past year. The substances examined included alcohol, marijuana, cocaine, heroin, hallucinogens, inhalants, and prescription opioids, and tranquilizers/sedatives (combined). If the participants answered positively to any criteria of abuse or dependence for these substances and specified their recent use in the past 12 months, they were categorized as past-year problematic users.

2.1.4. Past-year mental health and deviant behavior variables

Mental health variables included were past-year anxiety disorder and major depressive disorder (MDD), and serious psychological distress (SPD). MDD and anxiety disorder were assessed by participants' self-report of past-year diagnosis by a medical doctor or health care professional. SPD was measured using the K6 screening instrument for nonspecific psychological distress. For all survey years, participants were classified with past-year SPD if a score based on these K6 measures was 13 or greater (Kessler et al., 2003). Past-year mental health and substance abuse service use were ascertained by asking participants whether they received any mental health treatment or substance abuse treatment in the past year. Past-year deviant behaviors were assessed by asking the participants how many times they had attacked someone with the intent to seriously hurting them, how many times they had sold illegal drugs, and how many times they had stolen or tried to steal

anything worth more than $50. Consistent with past research (APA, 2013; SAMHSA., 2009), participants who reported any of the four behaviors were categorized as having "deviant behavior" (0 for none of these behaviors and 1 for engaging in one of more of these behaviors at least once). Past-year incarceration was assessed by asking the participants how many times in the past 12 months they had been arrested and charged with breaking the law without counting minor traffic violations (0 for none and 1 for at least once). Past-year sexually transmitted disease (STD) was also assessed by participant self-reports of diagnosis by a medical doctor or health care professional.

2.2. Statistical analyses

Complex latent class analysis (LCA) was used to identify subgroups according to concurrent problematic substance use among individuals who used ADHD stimulants in the past year. We performed LCA for 1 to 7 classes in order to ascertain the model with the optimal fit. Minimum values of the Bayesian Information Criterion (BIC) was given priority over other fit statistics such as Akaikes Information Criterion (AIC) and Sample Size Adjusted BIC (ABIC), given its more stable performance in simulation studies (Greenhill et al., 2002). We also considered the class size and clinical interpretability in selecting a model that would be applicable to the subsequent analysis of external validators.

LCA was applied using the Mplus software (Muthén, 2007). We chose eight dichotomous substance use variables (past-year problematic use of alcohol, marijuana, cocaine, heroin, hallucinogens, inhalants, and prescription opioid use, and

tranquilizers/sedatives) to empirically determine the smallest number of subtypes (classes) with similar drug use patterns that explain their response patterns. Once the number of classes was ascertained, correlates including socio-demographics, mental health and deviant behaviors were incorporated into the models using unadjusted and adjusted multinomial regression models. These analyses were conducted using both a modal assignment latent regression approach with Stata 13.0 software (StataCorp, 2013), and the newly introduced Mplus three step (R3Step) latent regression model (Asparouhov T, 2012). As the results of the two sets of analyses were consistent and some of the ORs obtained from the 3-step latent regression model were extremely large due to its instability in survey design, here we only present results from modal assignment model. All analyses included adjustment for the complex survey design by taking into account the survey weights, clustering and stratification. All the percentages reported are weighted. A $p<0.05$ was used to ascertain the statistical significance of findings.

3. Results

3.1. Characteristics of the nonmedical ADHD stimulant users (Table 1)

The frequency distribution of participant characteristics is presented in Table 1. Approximately 1.1% (n = 6,103) of adult participants from the NSDUH reported nonmedical use of ADHD stimulants in the past year. A relatively higher percent of nonmedical ADHD stimulant use was found among males (56.8%), young adults aged 18-25 (65.7%), whites (86.5%), those who had never married (79.0%), participants with some college experience or higher educational level (63.6%) and

with a household income < $20,000 (33.2%). Our adjusted logistic regression analyses further showed that they were more likely to report depression (aOR=1.25, 95%CI [1.02,1.53]), anxiety disorder (aOR=1.25, 95%CI [1.01,1.56]), serious psychological distress (aOR=1.55, 95%CI [1.40,1.72]), to have received mental health treatment (aOR=1.22, 95%CI [1.02,1.46]) and SUD treatment (aOR=2.27, 95%CI [1.84,2.81]), to report deviant behaviors (aOR=4.65, 95%CI [4.05,5.34]), incarceration (aOR=1.59, 95%CI [1.34,1.90]), and sexually transmitted disease (aOR=1.95, 95%CI [1.43,2.66]) in the past year.

3.2. Subtypes of nonmedical ADHD stimulant users by LCA (Figure 1)

The greatest proportion of problematic substance use among nonmedical ADHD stimulants users involved alcohol (64.2%), followed by marijuana (43.6%), cocaine (10.6%), tranquilizers and sedatives (8.8%), hallucinogens (8.4%), heroin (2.5%), inhalants (2.3%), and pain relievers (2.1%).

Latent class analysis was performed for 1 to 7 class models. The fit statistics of AIC (13942.5), BIC (14141.9) and ABIC (14030.7) were lower for the 4-class compared to the 3-class model (AIC=14018.1; BIC=14166.3; ABIC=14083.7) and similar to or lower to the 5-class model (AIC=13918.4; BIC=14169.1; ABIC=14029.3), suggesting that the minimum fit index values were obtained for the 4-class model (Greenhill et al., 2002). Whereas the Vuong-Lo-Mendel-Rubin (VLMR) test results supported a 2-class model, indicating a better fit (2-class: p=<0.0001; 3-class: p=0.2135). By taking into account the minimum value of BIC as well as the clinical interpretability, a 4-class model was selected (Appendix Table 3).

Figure 1 plots the past-year nonmedical ADHD stimulant use on the x-axis and the probability of past-year problematic use with each substance for the four classes as indicated on the y-axis. Class 1, which was the largest class and comprised 53.3% of the sample, was comprised of individuals with moderate probabilities of problematic use of alcohol (53.5%) and marijuana (21.6%) and near zero probabilities of other problematic substance use (class 1 - *Low substance class*, 53.3%). Class 2 made up 13.3% of the study sample and also consisted of individuals with moderate probabilities of problematic use of alcohol and marijuana, but additionally included participants with high probabilities of problematic use of pain relievers and sedatives/tranquilizers (class 2 - *Prescription drug class*, 13.3%). Class 3 included individuals with remarkably high probabilities of problematic use of marijuana and alcohol (class 3 – *Alcohol/marijuana class*, 28.8%). Finally, class 4 was comprised of individuals who had high probabilities of problematic use of most of the substances examined (class 4 - *Multiple substance class*, 4.6%).

3.3 Characteristic of participants in the LCA-defined classes (Table 2 and 3)

Table 2 presents the socio-demographic, mental health and deviant behavior profiles of the 4 classes of past-year nonmedical ADHD stimulant users. Prescription drug and Multiple substance classes showed particularly high prevalence of mental health problems such as major depression *(Prescription drug*: 30.6%; *Multiple substance*: 28.3%), anxiety disorder (*Prescription drug*: 28.2%; *Multiple substance*: 24.0%), serious psychological distress (*Prescription drug*: 52.4%; *Multiple substance*: 53.6%). Multiple substance class had exceptionally high prevalence of deviant behaviors (79.3%) and incarceration (33.3%). Results from the unadjusted

and adjusted latent regression models are presented in Table 3 which presents the odds ratios (ORs) and adjusted odds ratios (aORs) with class 1 (*Low substance class*) as the reference class. Relative to the Low substance class, being unemployed was associated with a greater odds of being in all of the other classes, while having some college education or higher (vs. less than high school education), being female, and being in the ≥ 26 years age class (vs. being in age class <26 years) were associated with lower odds of being in the *Alcohol/marijuana class* and *Multiple substance class*. Additionally, *Prescription drug class* participants were more likely to be older and no longer married relative to the Low substance class, which showed distinct profiles compared to *Alcohol/marijuana* and *Multiple substance classes*.

Compared with the Low substance class, unadjusted models showed that both the Prescription drug and Multiple substance classes were more likely to have psychiatric problems (major depression, anxiety disorder, serious psychological distress), to have a history of service use (mental health or substance service use) and to report deviant behaviors and incarceration. However, the *Alcohol/marijuana class* only had higher odds of past-year serious psychological distress, substance service use, deviant behaviors and incarceration compared to *Low substance class*. Nevertheless, with few exceptions, participants in class 2-4 were overall more likely to have all types of mental health problems, mental health and substance service use, deviant behaviors and incarceration even after adjusted for socio-demographics. The *Multiple substance class* additionally had higher odds of past-year sexually transmitted disease compared with the *Low substance class.*

4. Discussion

To our knowledge, this is the first study to examine concurrent problematic substance use patterns among adults who reported nonmedical ADHD stimulant use in a nationally representative sample. There are three main findings in this study. First, there exists a large subgroup (*Low substance class*) among the nonmedical ADHD stimulants users that simply had problematic moderate alcohol and marijuana use, which has not been reported in prior literature. Second, the other three subgroups including *Prescription drug class*, *Alcohol/marijuana class* and *Multiple substance class* all had high probabilities for mental health problems, service use, and deviant behaviors relative to the *Low substance class*. Third, participants in the 4 classes had distinct socio-demographic, mental health and service use profiles.

Consistent with previous literature, nonmedical ADHD stimulant users were more likely to report other substance use and risky behaviors compared to non-users (Arria et al., 2008; Herman-Stahl et al., 2007; McCabe et al., 2005; McCabe and Teter, 2007; Teter et al., 2005; Teter et al., 2006; White et al., 2006). Epidemiologic studies have found relationships between nonmedical use of prescription stimulants and presence of depressed mood among youth (Compton et al., 2006; Poulin, 2007; Teter et al., 2010). It is noteworthy that our study further found these users were more likely to have clinician-identified depression and anxiety and self-reported serious psychological distress with prior mental health treatment, even after adjustment for socio-demographic characteristics. It is possible that the stimulant users developed psychological problems after using the stimulants or used these drugs for self-medication (Khantzian, 1997). A previous study suggested that 39% of

college prescription stimulant use was for self-treatment (McCabe et al., 2009). Our finding underscores the significance of screening for mental health disorders among the nonmedical ADHD stimulant users.

Our study further documents the presence of considerable heterogeneity among nonmedical ADHD stimulant users. More than half of the nonmedical ADHD stimulant users comprised the Low substance class, which has the lowest prevalence of mental health problems and risky behaviors in the class of non-medical stimulant users. However, a large proportion (53%) of individuals in the Low substance class reported problematic alcohol use and 21.6% reported problematic marijuana use. This finding is consistent with a previous report also based on the NSDUH data indicating that college students who used Adderall® nonmedically were 3 times more likely to drink heavily and twice as likely to binge drink compared to nonusers (SAMHSA, 2009a). In view of the adverse physical, mental and social consequences of problematic alcohol use (Brown et al., 2000; Chesson et al., 2000; Hingson et al., 2009), greater attention to alcohol-related problems among this subgroup is needed.

Consistent with our hypothesis, *Prescription drug*, *Alcohol/marijuana* and *Multiple substance classes* were all more likely to report mental health problems, mental and substance abuse service use, and deviant behaviors compared to Low substance class. Furthermore, the three classes were all less likely to have college or higher education and were more likely to be unemployed compared to the Low substance class, indicating their relatively lower socio-economic status and fewer resources. These individuals are probably in greater need of both substance and mental health services as previous studies have shown that individuals with more

severe substance comorbidity tend to have greater unmet need for professional care (Chen et al., 2013; Wang et al., 2005).

The socio-demographic characteristics of the three classes with a greater number of concurrent problematic substance use differed. Whereas the *Alcohol/marijuana* and *Multiple substance class* were more likely to be younger, male and never married, the *Prescription drug class* were more likely to be older and no longer married. Past research has also found that individuals with tranquilizer or sedative abuse or dependence are generally middle-aged or older (Becker et al., 2008). In addition, the odds of having psychiatric comorbidity and service use in the *Alcohol/marijuana class* were much lower than those in *Prescription drug classes*; however, these two classes did not show remarkably different odds of having deviant behaviors and incarceration. This finding implies that the *Alcohol/marijuana class* may simply have high impulsivity but not a greater burden of mental health problems. In contrast, the *Prescription drug class* had a high probability of all mental disorders examined (depression: 30.6%, anxiety: 28.2%, serious psychological distress: 52.4%), which may be explained by the nonmedical use of opioids or tranquilizers/sedatives taken to self-medications for psychiatric symptoms (Becker et al., 2008; Joranson et al., 2000; Kreek and Koob, 1998).

Compared to the *Low substance class*, the *Multiple substance class* participants were significantly more likely to report mental health problems, mental and substance service use, behavior problems, and sexually transmitted diseases. Previous studies have shown that comorbid substance use and psychiatric disorders confer an additional risk for poorer outcomes and treatment response among opioid-

abusing patients (Strain, 2002; Volkow et al., 2002). Similarly, the use of alcohol in combination with other drugs is associated with more severe psychological and social consequences (Hasin et al., 2007; Hedden et al., 2009). A previous study pointed out that substance comorbidity is associated not only with greater odds of service use but also with higher perceived unmet service needs (Chen et al., 2013), indicating that more clinical resources should be available to this population.

This study has several strengths, including a large sample size and generalizability to the US household population. However, our findings should be interpreted in light of several limitations, mainly inherent to the NSDUH. First, the cross-sectional survey data limits assessment of temporal relationships and causal inferences. Second, two of the mental health measures (e.g. clinician-identified depression and anxiety) were subject to health care utilization. Third, we were not able to explore the motives and the trajectories of substance use which may offer significant implications for prevention. Lastly, all the information were based on self-report, which is vulnerable to recall and reporting biases, particularly for data on substance use and other sensitive behaviors. However, the validity of substance use has been established in a previous study (Harrison, 2007).

5. Conclusion

Our study provides evidence for 1) the existence of distinct subgroups of problematic substance users among adult nonmedical ADHD stimulant users; and 2) differences in the socio-demographic, health and behavioral profiles of these subgroups. Thus, differentiating concurrent substance use patterns among the users is

important for clinicians and public health policy makers. More than half of the users constitute the Low substance class, who while at risk for alcohol-related problems, are not at increased risk for using “hard drugs” or experiencing adverse health and social outcomes. The study also identified a Multiple substance class, which is a population that is in need of more resources due to larger number of problematic use of substances and higher severity of psychosocial consequences. Future studies which explore potential variations in sources of nonmedically used stimulants and the reasons for use of these drugs among these subgroups of stimulant users would provide clues to strategies to curb the problematic use of these drugs.

Table 1. Characteristics of past-year nonmedical ADHD stimulant users in a sample of the US population aged 18 and above (N= 6,103): data from 2006–2011 National Survey on Drug Use and Health.

Characteristics	**Nonmedical ADHD stimulant users N (Wgt%)**	**Adjusted odds ratios[a] (95% CI)**
Gender		
Male	3,369(56.8)	1.00
Female	2,734(43.2)	0.81(0.74,0.88)‡
Age		
18-25	5,347(65.7)	1.00
≥ 26	756(34.3)	0.25(0.22,0.29)‡
Race		
Non-Hispanic White	5,128(86.5)	1.00
Minorities	975(13.5)	0.26(0.22,0.30)‡
Marital status		
Married	372(12.6)	1.00
No longer married	229(8.3)	1.76(1.30,2.37)‡
Never married	5,502(79.0)	4.62(3.72,5.73)‡
Employment		
Full/Partial	4,136(69.8)	1.00
Unemployed	642(9.9)	1.01(0.84,1.22)
Not labor force	1,325(20.4)	0.85(0.74,0.97)*
Education		
< high school	794(11.2)	1.00
High school	1,648(25.2)	1.23(1.06,1.43)†
≥ College	3,661(63.6)	2.35(2.02,2.74)‡
Income		
< $20,000	2,425(33.2)	1.00
$20,000- $49,999	1,650(29.1)	0.72(0.64,0.82)‡
$50,000- $74,999	738(12.9)	0.63(0.54,0.74)‡
≥ $75,000	1,290(24.7)	0.72(0.63,0.83)‡
Past-year Depression		
No	5,160(84.8)	1.00
Yes	852(15.3)	1.25(1.02,1.53)*
Past-year Anxiety		
No	5,372(87.7)	1.00
Yes	731(12.3)	1.25(1.01,1.56)*
Past-year serious psychological distress		
No	4,345(70.8)	1.00
Yes	1,758(29.2)	1.55(1.40,1.72)‡
Past-year mental health treatment	4,743(75.8)	1.00
No	1,336(24.2)	1.22(1.02,1.46)*
Yes		
Past-year SUD treatment		
No	5,522(89.9)	1.00

Yes	581(10.1)	2.27(1.84,2.81)‡
Past-year deviant behavior		
No	4,065(70.9)	1.00
Yes	2,038(29.1)	4.65(4.05,5.34)‡
Past-year Incarceration		
No	5,152(86.3)	1.00
Yes	951(13.7)	1.59(1.34,1.90)‡
Past-year STD		
No	5,891(95.9)	1.00
Yes	212(4.1)	1.95(1.43,2.66)‡

Table 2. Characteristics of past-year nonmedical ADHD stimulant classes identified through latent class analysis in a sample of the US population aged 18 and above (N= 6,103): data from 2006–2011 National Survey on Drug Use and Health.

Characteristics, N (Wgt%)	Low substance users	Prescription drug users	Alcohol-marijuana users	Polysubstance Users
Total	2,995(53.3)	718(13.3)	2,064(28.8)	326(4.6)
Gender				
Male	1,556(54.6)	349(51.5)	1,271(62.4)	193(63.7)
Female	1,439(45.4)	369(48.5)	793(37.6)	133(36.3)
Age				
18-25	2,578(61.0)	558(50.1)	1,912(80.1)	299(75.6)
≥ 26	417(39.1)	160(49.9)	152(19.9)	27(24.5)
Race				
Non-Hispanic White	2533(86.4)	620(89.5)	1717(85.6)	258(84.3)
Minorities	462(13.6)	98(10.6)	347(14.4)	68(15.7)
Marital status				
Married	225(15.9)	73(18.4)	66(5.0)	8(6.4)
No longer married	107(8.3)	62(17.7)	46(4.4)	14(6.7)
Never married	2663(75.9)	583(63.9)	1952(90.6)	304(86.9)
Employment				
Full/Partial	2116(72.8)	459(65.7)	1376(67.9)	185(59.1)
Unemployed	214(7.6)	100(12.4)	249(11.2)	79(20.8)
Not labor force	665(19.7)	159(21.9)	439(21.0)	62(20.2)
Education				
< high school	271(8.8)	156(16.2)	282(11.6)	85(20.9)
High school	645(19.7)	238(33.8)	622(27.9)	143(47.6)
≥ College	2079(71.5)	324(50.0)	1160(60.6)	98(31.6)
Income				
< $20,000	1198(32.2)	240(27.4)	866(37.4)	121(35.6)
$20,000- $49,999	763(26.9)	249(39.3)	547(28.5)	91(29.9)
$50,000- $74,999	368(13.6)	92(10.8)	235(12.8)	43(11.0)
≥ $75,000	666(27.3)	173(22.5)	416(21.3)	71(23.5)
Past-year Depression				
No	2658(88.2)	502(69.4)	1778(87.6)	222(71.7)
Yes	299(11.8)	205(30.6)	249(12.4)	99(28.3)
Past-year Anxiety				
No	2749(91.6)	532(71.8)	1853(89.8)	238(76.0)
Yes	246(8.5)	186(28.2)	211(10.2)	88(24.0)
Past-year serious psychological distress				
No	2372(78.2)	367(47.6)	1448(71.6)	158(46.4)
Yes	623(21.8)	351(52.4)	616(28.4)	168(53.6)
Past-year mental health treatment				
No	2483(81.6)	417(52.9)	1640(78.0)	203(59.9)
Yes	502(18.4)	296(47.1)	418(22.0)	120(40.1)
Past-year SUD treatment				

No	2866(95.2)	573(74.5)	1852(90.3)	231(70.9)
Yes	129(4.8)	145(25.5)	212(9.7)	95(29.1)
Past-year deviant behavior	2497(84.6)	400(63.3)	1103(56.9)	65(20.7)
No	498(15.4)	318(36.7)	961(43.1)	261(79.3)
Yes				
Past-year Incarceration				
No	2715(90.6)	555(80.2)	1681(84.2)	201(66.7)
Yes	280(9.4)	163(19.8)	383(15.8)	125(33.3)
Past-year STD				
No	2905(95.7)	689(97.0)	1993(96.5)	304(90.4)
Yes	90(4.3)	29(3.0)	71(3.5)	22(9.6)

*p<0.05, †p<0.01, ‡ p<0.001

a. Adjusted model was adjusted for all variables included in this table.

Table 3. Comparison of classes of past-year nonmedical ADHD stimulant users identified through latent class analysis in a sample of the US population aged 18 and above (N= 6,103): data from 2006–2011 National Survey on Drug Use and Health.

Characteristics	***Prescription drug class* v.s *Low substance class***		***Alcohol/marijuana class* v.s *Low substance class***		***Multiple substance class* v.s *Low substance class***	
	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)
Gender						
Male	1.00	1.00	1.00	1.00	1.00	1.00
Female	1.13(0.87,1.44)	1.18(0.92,1.50)	0.72(0.60,0.87)†	0.74(0.62,0.89)†	0.68(0.49,0.95)*	0.74(0.52,1.04)
Age						
18-25	1.00	1.00	1.00	1.00	1.00	1.00
≥ 26	1.56(1.17,2.08)†	1.23(0.84,1.79)	0.39(0.29,0.51)‡	0.52(0.37,0.72)‡	0.51(0.30,0.84)*	0.71(0.38,1.31)
Race						
Non-Hispanic White	1.00	1.00	1.00	1.00	1.00	1.00
Minorities	0.75(0.42,1.34)	0.69(0.31,1.16)	1.07 (0.81,1.41)	1.01(0.77,1.33)	1.18(0.73,1.91)	1.03(0.63,1.68)
Marital status						
Married	1.00	1.00	1.00	1.00	1.00	1.00
No longer married	1.84(1.08,3.14)*	1.63(0.97,2.75)	1.68(0.87,3.26)	1.63(0.83,3.23)	2.02(0.43,9.50)	1.69(0.37,7.67)
Never married	0.72(0.47,1.11)	0.84(0.51,1.38)	1.77(2.45,5.81)‡	2.35(1.44,3.84)†	2.85(0.92,8.90)	2.16(0.78,6.89)
Employment						
Full/Partial	1.00	1.00	1.00	1.00	1.00	1.00
Unemployed	1.81(1.21,2.71)†	1.66(1.08,2.55)*	1.57(1.11,2.24)*	1.41(1.03,1.94)*	3.37(2.00,5.66)‡	2.55(1.56,4.17)‡
Not labor force	1.23(0.81,1.88)	1.23(0.83,1.83)	1.14(0.91,1.45)	1.05(0.83,1.31)	1.26(0.72,2.22)	1.10(0.62,1.95)
Education						
< high school	1.00	1.00	1.00	1.00	1.00	1.00
High school	0.93(0.63,1.39)	0.92(0.62,1.38)	1.07(0.80,1.45)	1.05 (0.79,1.39)	1.02(0.61,1.69)	1.04(0.61,1.78)
≥ College	0.38(0.24,0.61)‡	0.40(0.26,0.63)‡	0.64(0.47,0.88)†	0.66(0.50,0.86)†	0.19(0.11,0.32)‡	0.20(0.11,0.34)‡
Income						
< $20,000	1.00	1.00	1.00	1.00	1.00	1.00
$20,000- $49,999	1.72(1.27,2.32)†	1.53(1.10,2.12)*	0.91(0.75,1.11)	1.05(0.85,1.31)	1.01(0.64,1.59)	0.92(0.57,1.49)
$50,000- $74,999	0.93(0.62,1.39)	0.86(0.55,1.37)	0.81(0.62,1.06)	0.98(0.75,1.29)	0.73(0.43,1.26)	0.72(0.41,1.24)
≥ $75,000	0.97(0.68,1.39)	1.04(0.74,1.45)	0.67(0.54,0.83)‡	0.80(0.66,0.97)	0.78(0.47,1.30)	0.88(0.55,1.41)

Past-year Depression						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	3.28(2.39,4.51)‡	3.40(2.05,5.63)‡	1.05(0.76,1.45)	1.29(0.92,1.82)	2.93(1.88,4.57)‡	2.92(2.15,3.96)‡
Past-year Anxiety						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	4.25(2.93,6.15)‡	4.09(2.71,6.17)‡	1.23(0.89,1.71)	1.47(1.06,2.04)*	3.42(2.10,5.59)‡	4.15(2.56,6.74)‡
Past-year serious psychological distress						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	3.95(3.14,4.97)‡	3.54(2.76,4.54)‡	1.42(1.17,1.73)†	1.63(1.32,2.02)‡	4.15(2.92,5.89)‡	4.52(3.11,6.57)‡
Past-year mental health treatment						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	3.95(2.83,5.51)‡	3.95(2.78,5.62)‡	1.25(1.00,1.56)	1.51(1.08,2.10)*	2.97(2.09,4.22)‡	4.12(2.81,5.89)‡
Past-year SUD treatment						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	6.80(4.24,10.89)‡	5.99(3.82,9.41)‡	2.13 (1.46,3.11)‡	2.33(1.52,3.28)‡	8.15(4.77,13.94)‡	7.27(4.37,12.01)‡
Past-year deviant Behaviors						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	3.19(2.52,4.03)‡	3.07(2.37,3.97)‡	4.16(3.38,5.11)‡	3.67(3.03,4.43)‡	21.00(14.11,31.25)‡	16.59(11.03,24.96)‡
Past-year Incarceration						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	2.37(1.87,3.00)‡	2.03(1.54,2.67)‡	1.80(1.38,2.35)‡	1.53(1.17,1.99)‡	4.81(3.10,7.46)‡	3.36(2.14,5.28)‡
Past-year STD						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	0.68(0.36,1.31)	0.68(0.33,1.40)	0.81(0.46,1.42)	0.86(0.49,1.51)	2.37(1.16,4.84)*	2.95(1.47,5.95)†

a. Adjusted model was adjusted for gender, age, race, marital status, employment, education, and income for these variables. For mental health and deviant behaviors variables, adjusted model was adjusted for gender, age, race, marital status, employment, education, income, and the measured variable itself.

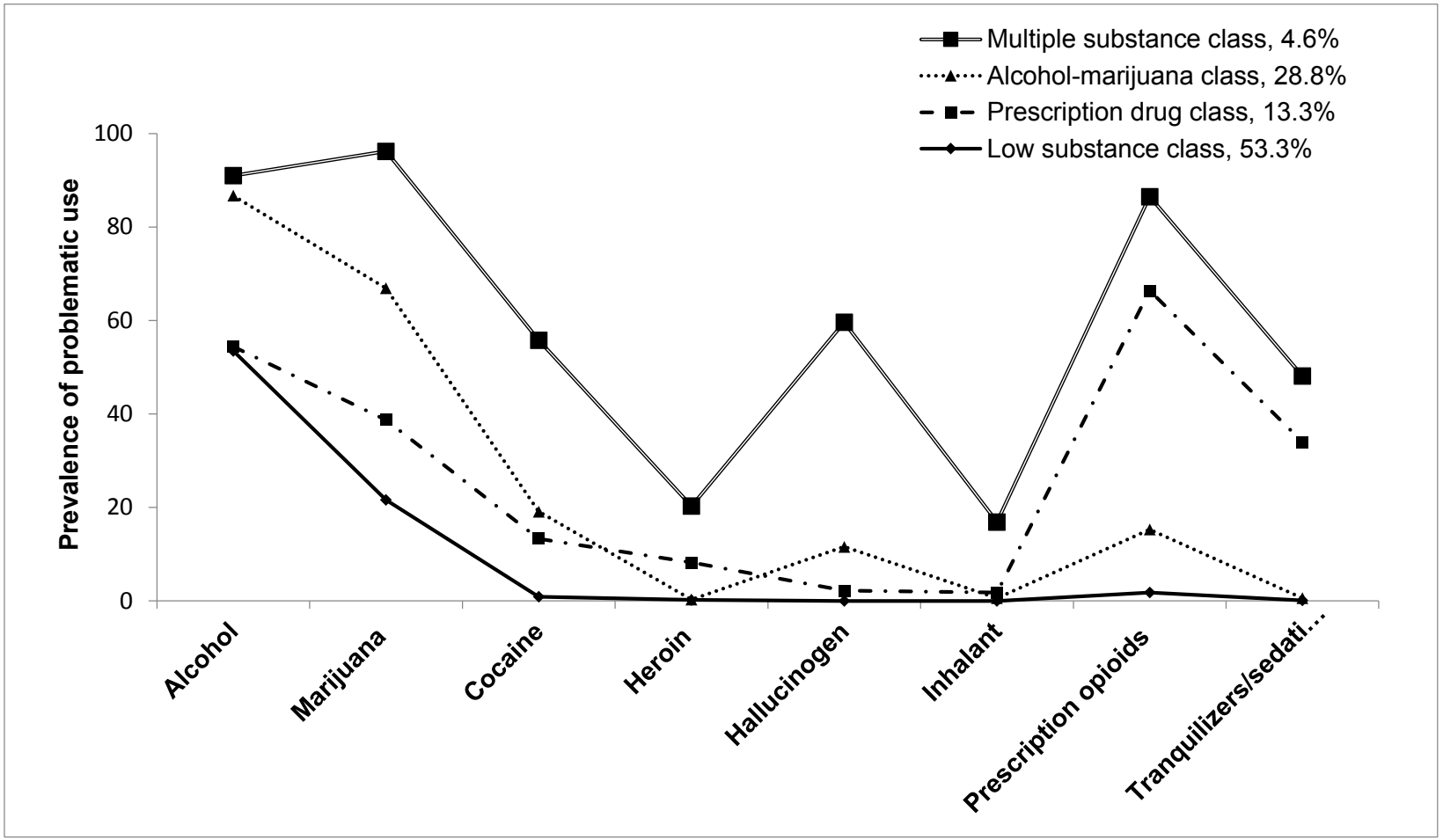

Figure 1. Conditional probabilities of problematic use of substances among 6,103 participants of 2006–2011 National Survey on Drug Use and Health with past-year nonmedical ADHD stimulant use categorized using latent class analysis.

Chapter 5: Discussion

This chapter will first present an overview of the key findings of each of the three studies. Study limitations and strengths will next be described, followed by a discussion of public health implications, and finally concluding remarks.

5.1. Overview of Main Findings

5.1.1. Aim 1 (Chapter 2)

The study described in Chapter 2 investigated the temporal trends of treatment visits, nonmedical use of, and ED visits for Adderall and methylphenidate among adults and adolescents from 2006 to 2011. The relationship between treatment visits, nonmedical use and ED visits were also examined using OLS regression model. While previous studies have implied the possibility that increased nonmedical ADHD stimulants use resulted from the increased availability (e.g. prescription) of ADHD stimulants (Cohen et al., 2006; McCabe and Boyd, 2005), our study showed that trends in treatment visits for stimulants did not correspond to trends of nonmedical use of these drugs. For instance, nonmedical Adderall use grew remarkably among adults while Adderall treatment visits remained stable. In addition, although friends or relatives were the major source of nonmedically used stimulants, up to two-thirds of these friends or relatives obtained their medications through legitimate prescriptions from physicians, regardless of age groups. These results suggest that increased drug diversion instead of increased availability may play a role in the increased trend of nonmedical ADHD use among adults. This study also found that adult ED visits involving Adderall was strongly correlated with increased nonmedical use in adults, suggesting the adverse health consequences tied

to nonmedical use. The findings of this study underscore the importance of preventive strategies to target at possible drug diversion trajectories as well as the urgent need of public health campaign to educate stimulant users regarding the physical hazards of these drugs.

5.1.2. Aim 2 (Chapter 3)

The study described in Chapter 3 aimed to examine the role of source of misused stimulants in nonmedical use of prescription stimulants. Previous studies have found that a friend or relative was the major source for the nonmedically used prescription stimulants (DeSantis and Hane, 2010; Garnier-Dykstra et al., 2012; McCabe et al., 2006b; White et al., 2006). This study further used medication source as a predictor to characterize the socio-demographics, psychological and behavioral profiles of nonmedical prescription stimulant users. In addition, the relationship between sources and the onset, recency, severity of stimulant use was examined. Consistent with previous studies, the most common source of these stimulants was a friend and relative, followed by physician source and illegal source. The results found that participants reporting different sources had different risk profiles: those of physician source had higher mental health burden while those of illegal source reported more behavioral problems. Physician source group had high odds of reporting early onset, recent use, frequent use and stimulant use disorders while illegal source group reported only early onset, frequent use and stimulant use disorders. Future efforts should be made to assure physicians to be equipped with sufficient training to identify these nonmedical users, the possible diversion behaviors, and high comorbid mental health problems. Illegal source group who had

lower socio-economic status and higher behavioral problems should be allocated with more clinical and social resources.

5.1.3. Aim 3 (Chapter 4)

The study described in Chapter 4 aimed to use latent class analysis (LCA) to identify heterogeneous subgroups of past-year nonmedical use of ADHD stimulant users by their concurrent problematic substance use. 2006-2011 NSDUH was used and subgroup analysis (adolescents v.s. adults) was also performed. Among adults, a four class model had the best model fit. These included *Low substance class* (53.3%), *Prescription drug class* (13.3%), *Alcohol/Marijuana class* (28.8%), and *Multiple substance class* (4.6%). Regression results showed that adult participants in the *Prescription drug class* and *Multiple substance class* had higher mental health burden and behavior problems than *Low substance class* while those in the *Alcohol/Marijuana class* only showed higher behavior problems. Among adolescents, a four class model was chosen, which included *Low substance class* (30.7%), *Prescription drug class* (16.9%), *Alcohol/Marijuana class* (44.1%), and *Multiple substance class* (8.3%). Regression results showed that compared to Low substance class, adolescent participants in other three classes all showed higher odds of major depression and behavior problems. This is the first study to show that nonmedical prescription stimulant users are a heterogeneous group with a large subgroup rarely having any problematic use of other substances. These subgroups have distinct patterns of mental health comorbidity, behavior problems and service use, with implications for prevention and treatment of nonmedical stimulant use, which also differed in different age groups. The findings can offer implications to

develop a more targeted preventive strategy for clinicians and policy makers to curb prescription stimulant misuse.

5.2. Study Limitations

These findings should be interpreted in light of several limitations. First, we utilized NSDUH from aim 1 to aim 3, which has brought inherent limitations the three studies. NSDUH is a cross-sectional survey dataset, limiting further assessment of temporal relationship and causal inference of nonmedical prescription stimulant use and other psychiatric or behavior problems examined. Also, all the information in NSDUH was based on self-report, which is open to social-desirability or recall bias. In addition, NSDUH is a household representative surveys which may fail to capture the homeless and jailed population, which were known to have even higher prevalence of substance use disorders (Department of Housing and Urban Development, 2011; Peters et al., 1998). Another limitation of this study lies in the limited available survey years in NSDUH data: questions regarding nonmedical use of Adderall were not added until year 2006. The available years so far (2006-2010) may not provide enough data for trend analysis, although we plan to add future survey years as they become available.

In the aim 1 study, we used three national representative surveys (NDTI, NSDUH, and DAWN) which were not linked to each other. Thus, the interpretation of the findings should be viewed in an ecological perspective. For example, we found that an increased trend of nonmedical Adderall use and that of ED visits involving Adderall among adults. However, we were not able to assess if those who visited ED

received Adderall through a physician's prescription. Also, any shifts in medical care policy or in drug market share which might impact the treatment visits of specific stimulants cannot be captured by these data. Additionally, treatment visits for methylphenidate and Adderall cannot directly represent the availability of these medications since the information of other sources cannot be obtained. Lastly, both NDTI and DAWN rely on physicians' reports, which may be vulnerable to recall bias.

The NSDUH was used in the aim 2 study; thus, there existed other limitations in addition to above-mentioned ones. For instance, the NSDUH asks for the most recent source of misused stimulant instead of most commonly used, which may not be the same. Also, this study could not capture those who reported multiple sources of these stimulants. Another limitation is that those who used Adderall only were not asked regarding their sources due to Adderall was added to the NSDUH questionnaire later on. Last, given the cross-sectional nature of the NSDUH, causal-relationship of nonmedical stimulant use and other psychiatric or stimulant use problems is hard to be established.

The major limitations lying in aim 3 study were tied to NSDUH design. Thus, cross-sectional survey as well as self-report bias was the major limitation. However, it should be noted that the mental health measures (e.g. clinician-identified depression and anxiety) examined in this study were subject to health care utilization, which cannot be generalized to the population without medical coverage. Also, the motives and the trajectories of nonmedical prescription stimulant use and other

mental or substance use were unknown, which may offer significant implications for prevention.

5.3. Study Strengths

Offsetting the aforementioned limitations are several strengths. First, NSDUH, used in all three aims, has the advantage of a large sample size and generalizability to the US household population. Similarly, the other datasets such as DAWN, NDTI, and NSCH all have such strengths. Second, this study attempts to examine the role of prescriptions in nonmedical use of prescription stimulants by conducting the trend analysis (aim 1) and the source of misused stimulants (aim 2), which can offer different perspectives of this issue. Third, that this study conducted subgroup analysis for adolescents (aged 12-17) and adults (aged 18 and above) while most of previous studies focus on college age population (McCabe et al., 2005; McCabe et al., 2006b; SAMHSA, 2009a; Teter et al., 2005; Teter et al., 2006) or adolescents (Herman-Stahl et al., 2007; Johnston, 2003; McCabe et al., 2007a). Fourth, this study, to my knowledge, is also the first to report state-level estimates of nonmedical prescription stimulant use. Fifth, this is also the first study to explore the heterogeneity of subgroups of nonmedical prescription stimulant users by concurrent substance use, which provides a unique opportunity to develop a more targeted preventive strategy to curb the misuse of these stimulants. Together, this study offered a comprehensive picture of nonmedical prescription stimulants including temporal trends, sources of medications, and users' profiles and aimed to examined the role of prescriptions in nonmedical use, which can which could offer major

implications in our understanding of the etiology and possibly prevention of nonmedical ADHD stimulant use by health professionals and policy makers.

5.4. Public Health Implications

The three aims in this study can complement previous research and offer significant public health and clinical implications. There are mainly three possible strategies which could help in reducing the epidemics of nonmedical prescription stimulants use. The first one and the most important step, is to develop clinical and preventive program targeting at drug diversion. Given that our aim 1 study showed that physicians constituted two-thirds of the source of the misused stimulants and nonmedical Adderall use increased without the treatment visits increasing accordingly, drug diversion may be an important way for the nonmedical prescription stimulant users to obtain their drugs. Thus, there is an urgent need for public health campaigns to 1) educate the users and the dispensers about the legal responsibility of misusing or diverting the medications; 2) educate our physicians to increase their vigilance regarding possible diversion of these medications.

Second, a more targeted preventive or treatment program should be developed. Our aim 1 and aim 3 both demonstrated that the temporal trends and users' profiles of nonmedical prescription stimulant users differ in adolescents and adults. Our aim 3 further showed that the users consisted of very distinct subgroups with different substance and psychiatric comorbidities, with a large group (Low substance class) consuming minimal illegal substances other than prescription stimulants. This subgroup may well respond to a public health campaign which can

dilute the illusion that "use of prescription drugs is safe". Meanwhile, the Multiple substance class (in aim 3) which have numerous problematic substance uses and carry more mental health burden, require more clinical resources, knowing that worse outcome or treatment response may be expected (Hasin et al., 2007a; Strain, 2002b; Volkow et al., 2002).

Third, our aim 2 offers evidence that source of misused stimulants could be a significant indicator of stimulant use problems, including onset, frequency and severity. Those who obtained medication from physicians carried more psychiatric risks and also had higher odds of poor indicators of stimulant use problems (e.g. early onset, recent use, and stimulant use disorder). Efforts should be made to develop a physician training program which helps to recognize the misuse and diversion among patients. In addition, since illegal source group had higher odds of risky behaviors and incarceration, efforts to curb stimulant misuse in this population should also criminal justice officials and government regulatory agencies to reduce the availability of these stimulants in the black market. A tailored preventive program should be developed taking into consideration of different sources of misused medications.

5.5. Future directions

Given the proven therapeutic efficacy of prescription stimulants for the treatment of ADHD (Goldman et al., 1998), there is a need to balance between the medical necessity of these drugs and the risks associated with nonmedical prescription stimulant use. Further research should be conducted to better understand

the trajectory of the nonmedical users, the pathway of diversions, and the impact of national or state-level policy.

As my aim 1 study offers a recent temporal trend of nonmedical use of prescription stimulants for different stimulants among different population, a valuable next step will be repeated and regular evaluation of these trends especially after Prescription drug Abuse Prevention Plan was implemented in 2011 by the Obama Administration (The White House). Since my three aims focused on national data from 2006 to 2011, whether the problem of prescription stimulant misuse can be curbed after 2011 can be an indicator of the effectiveness of this prevention plan.

Although my aim 2 illustrated the individuals obtained the misused stimulants via different sources had different psychiatric and behavioral risk profiles and different level of stimulant use problems. Efforts should be put to further understand the pathways of drug diversion from the dispensers' side and the trajectory of nonmedical prescription stimulants from the users' side. The following questions need to be answered: 1) What proportion of those who get legitimate prescriptions will divert their medications and what is the risk factor for them to divert the drugs? 2) How do drug dealers acquire their inventories of prescription stimulants from clinicians, hospitals/clinics, pharmacies and even patients? 3) When do the stimulant users develop other substance use or other mental health problems? A longitudinal study which can better delineate the causal relationship should be conducted, which could also help explain the heterogeneity of the nonmedical prescription stimulant users we demonstrated in aim 3.

Finally, the most important step involves efforts to dissemination of the findings to clinicians, educators, policy makers, and even general population, as discussed in the previous implication section. They included 1) public health campaigns to inform the general public about the risk of stimulant misuse; 2) education programs to encourage school teachers, clinicians, parents to be alert of possible drug diversion and to educate the drug diverters of their legal risks; 3) policy makers should be aware that there exist a group of nonmedical prescription stimulant users with other substance and mental problems who require more clinical resources. Thus, translating the research findings into practice is critical.

5.6. Conclusions

In summary, our three aims offer a global picture of nonmedical prescription stimulants in temporal trends, various sources, and users' profiles. Although aim 1 showed trends of nonmedical use does not correspond to the trends of treatment visits, aim 2 provided evidence that physician source group has poor outcome of stimulant use problems and higher psychiatric comorbidities. As physician is the major source of stimulants used nonmedically across age groups, drug diversion should be targeted as a preventive strategy. Aim 3 identified the heterogeneous subgroups existing in nonmedical prescription stimulant users, which calls for a more tailored preventive or treatment program. Thus, efforts should be made to bring the findings of this study into practice or policy and further in-depth research should be done in the future.

APPENDICES:

Table 1-1. Temporal trend of prescription, nonmedical use and emergency department (ED) visits of Adderall and methylphenidate using quarterly data in a community sample of the U.S. population aged 12 to 17.

	Adderall			Methylphenidate		
	Prescription	Nonmedical use	ED visits	Prescription	Nonmedical use	ED visits
Coeffi cient	-9.240	-0.008	0.006	-3.47	-0.040	0.0059
SE	1.570	0.010	0.022	0.68	0.006	0.0130
F test	0.000	0.454	0.787	0.000	0.000	0.648

Table 1-2. Temporal trend of prescription, nonmedical use and emergency department visits of Adderall and methylphenidate using quarterly data in a community sample of the U.S. population aged 18 and above.

	Adderall			Methylphenidate		
	Prescription	Nonmedical use	ED visits	Prescription	Nonmedical use	ED visits
Coeffi cient	-1.220	0.023	0.024	0.134	0.002	0.002
SE	1.580	0.004	0.003	1.330	0.003	0.001
F test	0.450	0.000	0.000	0.921	0.557	0.244

a. LMR stands for Lo-Mendel-Rubin test.

Table 2. Fit statistics of latent class analysis of nonmedical ADHD stimulant users based on concurrent problematic substance use for the 2-6 class models using a community sample of the U.S. population aged 12-17.

Classes	Entropy	-2LL	AIC	BIC	Adjusted BIC	LMR[a]
2	0.701	1260.570	14221.541	14318.400	14264.388	0.0000
3	0.737	221.421	14018.120	14166.257	14083.651	0.0324
4	0.650	93.587	13942.533	14141.948	14030.748	0.3284
5	0.692	42.133	13918.400	14169.094	14029.299	0.6341
6	0.659	35.449	13899.021	14200.993	14032.604	0.6233

Table 3. Fit statistics of latent class analysis of nonmedical ADHD stimulant users based on concurrent problematic substance use for the 2-5 class models using a community sample of the U.S. population aged 18 and above.

Classes	Entropy	-2LL	AIC	BIC	Adjusted BIC	LMR[a]
2	0.721	2073.411	33031.820	33146.002	33091.980	0.0000
3	0.578	285.482	32764.339	32938.969	32856.348	0.2135
4	0.576	254.720	32527.619	32762.697	32651.477	0.4344
5	0.664	49.746	32495.873	32791.401	32651.581	0.5304

a. LMR stands for Lo-Mendel-Rubin test.

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CURRICULUM VITAE
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EDUCATION & TRAINING

Period	Degree/Program	Institution	Field of Study
2010 – 2014	Ph.D.	Department of Mental Health, Johns Hopkins Bloomberg School of Public Health	Substance Abuse and Psychiatric Epidemiology
2009 - 2010	Chief Resident	Taipei City Psychiatric Center, Taiwan	Psychiatry
2006 - 2010	Residency	Taipei City Psychiatric Center, Taiwan	Psychiatry
1998-2006	M.D.	National Cheng-Kung University, Taiwan	Medicine
2004	Exchange Clerkship	Duke University Medical Center	Medicine

LICENSURE AND BOARD CERTIFICATION

Advanced Cardiovascular Life Support License, Taiwan, 2014
National Board of Psychiatric Medicine, Taiwan, 2010
Medical License, Taiwan, 2006

AWARDS & HONORS

Lucy Shum Award, Johns Hopkins Bloomberg School of Public Health, 2014
Sommer Scholarship, Johns Hopkins Bloomberg School of Public Health, 2012-
NIDA Women & Sex/Gender Junior Investigator Travel Award for meeting of the College on Problems of Drug Dependence (CPDD), 2012
Government Scholarship to Study Abroad, Ministry of Education, Taiwan, 2009
Clinical Excellence Award, Taipei City Psychiatric Center, Taiwan, 2008
Scholarship for Exchange Clerkship in Duke University Medical Center, 2004
Scholar Award, Schering-Plough Award for Medical Student Research, 2001

PRESENTATIONS

Oral Presentation

Chen LY, Alexandre PK & Martins SS. Correlates of nonmedical use of Adderall® in the United States. Oral presentation at 73rd annual meeting at College Problem on Drug Dependence. Hollywood, Florida. June 21st, 2011.

Poster Presentation

Chen LY, Crum RM, Strain EC, Kaufmann CN, Alexander GC, & Mojtabai R. Patterns of concurrent substance use among prescription stimulant misusers: Results from the National Survey on Drug Use and Health (NSDUH). Poster to be presented presentation at 76th annual meeting of College Problem on Drug Dependence on June 17, 2014

Chen LY, Kaufmann CN, Alexander GC, Mojtabai R, Martins SS. Correlates of nonmedical use of ADHD stimulants versus nonmedical use of other stimulants in a U.S.
national sample. Poster presentation at 29th International Conference on Pharmacopidemiology and Therapeutic Risk Management, Montréal Convention Center,
Montréal, Canada. August 28, 2013.

Kaufmann CN, **Chen LY**, Spira AP, Canham SL, Alexander GC, Mojtabai R. Trends in
the use of non-benzodiazepine sleep-aid medications in the United States, 1996-2010.
Poster presentation at 29th International Conference on Pharmacopidemiology and Therapeutic Risk Management, Montréal Convention Center, Montréal, Canada. August
28, 2013.

Kaufmann CN, **Chen LY**, Crum RM, Mojtabai R. Treatment Seeking and Barriers to Treatment for Alcohol Use in Persons with Alcohol Use Disorders and Comorbid Mood
or Anxiety Disorders. Poster presentation at 75 the annual meeting at College Problem on
Drug Dependence. San Diego, California. June 16, 2013.

Kaufmann, CN, Mojtabai R, Hock RS, Thorpe R, Canham SL, **Chen LY**, Spira AP. Racial/ethnic differences in trajectories of insomnia Severity among older adults: Results
from the Health and Retirement Study. Poster presented at SLEEP 2013 Meeting, Baltimore, Maryland. June 5, 2013.

Chen LY, Crum RM, Martins SS, Mojtabai R & Strain EC. Gender differences in substance use and mental health service utilization among persons with substance use disorders with vs. without comorbid major depression. Poster presentation at 74 the annual meeting at College Problem on Drug Dependence. Palm Spring, California. June 12, 2012.

Chen LY, Crum RM, Martins SS & Mojtabai R. Service use and barriers to mental health care in major depression and comorbid substance use disorders. Poster presentation at the 165 the Annual Meeting of American Psychiatric Association. Philadelphia, PA, May 9, 2012.

Martins SS, **Chen LY**, Fenton M, Keyes KM & Storr CL. Nonmedical prescription opioid use and use disorders secondary to nonmedical use among U.S. young adults by educational attainment. Poster to be presented at the 50th annual meeting at American College of Neuropsychopharmacology. Hawaii, Dec 2012.

Chen LY & Huang MC. Disulfiram induced hypersensitivity----a case report. Poster presentation at the 47th Annual Meeting of Taiwanese Society of Psychiatry. Taiwan. 2008.

Chen LY & Huang MC. Remarkable urinary tract symptoms associated with chronic ketamine abuse: two cases reports. Poster presentation at the 47th Annual Meeting of Taiwanese Society of Psychiatry. Taiwan. 2008

Chen LY & Lin SK. Ziprasidone augmentation in the treatment of refractory obsessive-compulsive disorder and schizophrenia: A case Report. Poster presentation at the 46th Annual Meeting of Taiwanese Society of Psychiatry.Taiwan. 2007.

Chen LY & Lin SK. Empirical experiences of rivastigmine in the treatment of benzodiazepines tolerance: Two cases reports. Poster presentation at the 46th Annual Meeting of Taiwanese Society of Psychiatry. Taiwan. 2007.

PUBLICATIONS

Chen LY, Crum RM, Strain EC, Kaufmann CN, Alexander GC, & Mojtabai R. National Variation of ADHD Medication treatment and nonmedical ADHD medication use. In preparation.

Chen LY, Strain EC, Crum RM, Storr C, & Mojtabai R. Sources of Nonmedically Used Prescription Stimulants: Differences in Recency and Severity of Misuse in a Population-Based Study. Under review.

Chen LY, Crum RM, Strain EC, Kaufmann CN, Alexander GC, & Mojtabai R. Prescriptions, nonmedical use, and ER visits of prescription stimulants. Under review.

Chen LY, Crum RM, Martins SS, Kaufmann CN, Strain EC, & Mojtabai R. Patterns of concurrent substance use among nonmedical ADHD stimulant users: Results from the National Survey on Drug Use and Health. In press, Drug and Alcohol Depend. 2014 June.

Martins SS, Levin D, **Chen LY**, Keyes KM, Magdalena Cerdá M, Storr CL. Nonmedical Prescription Opioid Use and Use Disorders secondary to Nonmedical Use among U.S. Young Adults by Educational Attainment. Under review.

Eaton WW, **Chen LY**, Dohan FC, Kelly DL, Cascella N.A Case Study of Schizophrenia and Immune Reaction to Gluten. Under review.

Chen LY, Strain EC, Alexandre PK, Alexander GC, Mojtabai R, Martins SS. Correlates
of nonmedical use of stimulants and methamphetamine use in a national sample. Addict Behav. 2014 Feb 12;39(5):829-836.

Chen LY, Strain EC, Crum RM, & Mojtabai R. Gender differences in substance abuse
treatment and barriers to care among persons with substance use disorders with and without comorbid major depression. J Addict Med. 2013 Sep-Oct;7(5):325-34.

Chen LY, Crum RM, Martins SS, Kaufmann CN, Strain EC, & Mojtabai R. Service use
and barriers to mental health care in major depression and comorbid substance use disorders. Psychiatr Serv. 2013 Sep 1;64(9):863-70.
Kaufmann CN, **Chen LY**, Crum RM, Mojtabai R. Treatment seeking and barriers to treatment for alcohol use in persons with alcohol use disorders and comorbid mood or
anxiety disorders. Soc Psychiatry Psychiatr Epidemiol. 2013 Jul 31. [Epub ahead of print].
Mojtabai R, **Chen LY**, Kaufmann CN, Crum RM. Comparing barriers to mental health
treatment for alcohol use in persons with alcohol use disorders and comorbid mood or
anxiety disorders. J Subst Abuse Treat. 2014 Feb;46(2):268-73.
Chen LY, Chen KP, Huang MC. Cystitis associated with chronic ketamine abuse. Psychiatry Clin Neurosci. 2009 Aug ; 63(4):591.
Chen LY, LI Hor. Determination of the role of cytotoxicity in Vibrio vulnificus virulence in mice by characterizing of a noncytotoxic mutant. A medical thesis. 2004.

EDITORIAL ACTIVITIES
Peer Review Activities
Addictive behaviors - 2013 - present
British Medical Journal, Psychiatry - 2013 - present
Psychopharmacology-2013-present

RESEARCH ACTIVITIES
Prescription stimulants: temporal trends, geographical variations, and heterogeneity of the nonmedical users, 2013-2014.
Correlates of nonmedical use of stimulants and methamphetamine use in a national sample, 2012-2013.
Gender differences in substance use and mental health service utilization among persons
with substance use disorders with vs. without comorbid major depression, 2011-2012.
Service use and barriers to mental health care in major depression and comorbid substance use disorders, 2011-2012.
Correlates of illegal drugs use and nonmedical use of Adderall® in the United States, 2010-2011.
Factors associated with MMT retention in Northern Taiwan among heroin users enrolled
in methadone treatment in northern Taiwan, 2010-2011.
The urology and CNS consequences post ketamine dependence, 2008- 2009.

TEACHING ACTIVITIES

"Perspective of Psychiatry: The public health framework", 2012/ August-November, Johns Hopkins Bloomberg School of Public Health
Instructor: Paul R McHugh, MD, Professor
Alan J Romanoski, MD, MPH, Associate Professor
Teaching assistant: Lian-Yu Chen

"Introduction to mental health service", 2014/ March-May, Johns Hopkins Bloomberg School of Public Health
Instructor: Ramin Mojtabai, MD, Associate Professor
Teaching assistant: Lian-Yu Chen

PROFESSIONAL SOCIETIES
Center Affiliates of Center for drug and safety in Johns Hopkins Bloomberg School of Public Health, 2012-date
Taiwanese Society of Addiction Science, member, 2008- date
Center for Development of Psychotherapy, member, Taiwan, 2007- date
Taiwanese Society of Psychiatry, member, 2006- date

SCIENTIFIC MEETINGS
29th International Society for Pharmacoepidemiology, Montreal, Canada, 2013
74th annual meeting at College Problem on Drug Dependence, California, USA, 2012
165th annual meeting at American Psychiatric Association, Philadelphia, USA, 2012
73rd annual meeting at College Problem on Drug Dependence, Florida, USA, 2011
2nd World Congress of Asian Psychiatry, Taipei, Taiwan, 2010
49th Annual Meeting of Taiwanese Society of Psychiatry, Taipei, Taiwan, 2010
48th Annual Meeting of Taiwanese Society of Psychiatry, Tainan, Taiwan, 2009
47th Annual Meeting of Taiwanese Society of Psychiatry, Taipei, Taiwan, 2008
46th Annual Meeting of Taiwanese Society of Psychiatry, Kaohsiung, Taiwan, 2007

LEARDERSHIP EXPERIENCES
Behavioral Health International Group (BHIG) in JHSPH, member, 2010- date.
2nd World Congress of Asian Psychiatry, Host. Taipei, Taiwan, 2010
Anti-AIDS Condom Delivery Street Campaign, Host and organizer. Taiwan, 2003.
National delegate in General Assembly of International Federation of Medical Student Association (IFMSA). Former Yugoslavia, 2003.
Federation of Medical Student Association in Taiwan (IFMSA) Standing Committee on Reproductive Health & AIDS (SCORA), National local officer, 2002-2003.
National delegate in East Asian Medical Students' Conference, Taiwan, 2002.
Speech and Debate Club of National Chung Kung University, president, Taiwan, 2001-2002.
Literature Club of National Chung Kung University, vice president, Tainan, Taiwan, 2001.

SKILLS

Languages: Fluent in Taiwanese, Mandarin Chinese and English
Technical: Stata, Microsoft Office, Mplus, GIS